CYCLOMETALATED RHODIUM COMPLEXES FOR SELECTIVE TRANSFER HYDROGENATION

Thesis submitted in accordance with the requirements of the University of Liverpool for the degree of Doctor in Philosophy

by

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In memory of my dear **FATHER**, and to all my **TEACHERS**, at every level of my education, your great work has brought me this far. I remain forever grateful.

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ABSTRACT

Selective transfer hydrogenation of aldehydes and α,β-unsaturated carbonyl compounds is some of the most attractive and challenging transformations found in both industry and academia. However, the chemo-selective reduction of such compounds is challenging, especially when methanol is employed as the source of hydrogen and the reaction solvent. My thesis contributes to the development of new rhodium catalysts that enable the use of abundant and easy-to-handle methanol for the reduction of aldehydes and α,β-unsaturated carbonyls with high selectivity under mild reaction conditions.

Chapter 1 provides an introduction covering the area of transfer hydrogenation of C=X (X = C, O) bonds, and the use of methanol as a hydrogen donor. It also describes previous cyclometalated complexes and their recent developments in the area of transfer hydrogenation, including the previous work that has been developed by our group.

Chapter 2 describes the use of rhodium complexes "rhodacycles" for the selective transfer hydrogenation of a wide range of aromatic aldehydes in the presence of various sensitive functional groups. The reduction was carried out using methanol as both the reaction solvent and hydrogen donor.

Chapter 3 follows the successful reduction of the aldehydes, presenting a rhodium complex that has shown to be capable of the selective reduction of the C=C double bond moiety within α,β-unsaturated ketones to give corresponding saturated ketones. Substituted chalcones and benzylideneacetophenones are efficiently reduced under this catalytic system.

Chapter 4 is an expansion of Chapter 3. The rhodium complex shows high efficiency for the transfer hydrogenation of α,β-unsaturated aldehydes at room temperature with the use of methanol as a source of hydrogen.

Chapter 5 establishes a new method for the selective reduction of mono- and di-aldehydes. A rhodium complex has been found to be highly effective for the selective reduction of mono- and di-aldehydes under mild reaction conditions using formic acid as a hydrogen source.

Chapter 6 presents the conclusion and the perspectives of all the work covered in this thesis.

LIST OF PUBLICATIONS

- **Methanol as hydrogen source: transfer hydrogenation of aromatic aldehydes with a rhodacycle**

  A. H. Aboo, E. L. Bennett, M. Deeprose, C. M. Robertson, J. A. Iggo and J. Xiao, *Chem. Commun.*, 2018, **54**, 11805–11808.

- **N,O- vs N,C-Chelation in Half-Sandwich Iridium Complexes: A Dramatic Effect on Enantioselectivity in Asymmetric Transfer Hydrogenation of Ketones**

  G. Zhou, A. H. Aboo, C. M. Robertson, R. Liu, Z. Li, K. Luzyanin, N. G. Berry, W. Chen and J. Xiao, *ACS Catal.*, 2018, **8**, 8020–8026.

- **A Convenient Procedure for the Oxidative Dehydrogenation of N-Heterocycles Catalyzed by FeCl2/DMSO**

  W. Zhou, P. Taboonpong, A. H. Aboo, L. Zhang, J. Jiang and J. Xiao, *Synlett*, 2016, **27**, 1806–1809.

ABBREVIATIONS

α	Alpha
β	Beta
δ	Delta (NMR chemical shift)
Å	Angstroms
aq	Aqueous
Ar	Aryl
atm	Atmosphere
BnOH	Benzyl alcohol
bs	Broad singlet
°C	Celsius degree
^{13}C	Carbon 13
Cat.	Catalyst
CDH	Catalytic dehydrogenation
CD_3OD	Deuterated methanol
CI	Chemical ionisation
cm	Centimetre(s)
COD	1,5-Cyclooctadiene
conv.	Conversion
Cp*	Pentamethylcyclopentadiene
Cy	Cyclohexyl
d	Doublet
dd	Doublet of doublets

dppp	1,3-Bis(diphenylphosphino)propane
dt	Doublet of triplets
DCM	Dichloromethane
eq	Equation
et al.	and others
equiv.	Equivalent(s)
F/T	Formic acid/triethylamine azeotrope
g	Gram(s)
h	Hour(s)
^{1}H	Proton
H_2	Molecular hydrogen
HRMS	High resolution mass spectroscopy
Hz	Hertz
i.e.	*id est* (that is to say)
IR	Infrared
J	Coupling constant value
K	Degree Kelvin
m	Meta
m	Multiplet
Me	CH_3
MeOH	Methanol
mg	Milligram(s)
min	Minute(s)
mL	Millilitre

mmol	Milimole(s)
MS	Mass spectrometry
NEt_3	Triethylamine
NMR	Nuclear magnetic resonance
o	Ortho
p	Para
Ph	C_6H_5
PhMe	Toluene
ppm	Parts per million
q	Quartet
Rh	Rhodium
r.t.	Room temperature
s	Singlet
sept	Septet
td	Triplet of doublets
TFE	2,2,2-tifluoroethanol
TH	Transfer hydrogenation
THF	Tetrahydrofuran
TMS	Tetramethylsilane
TsDPEN	*N*-(*p*-toluenesulfonyl)-1,2-diphenylethylenediamine

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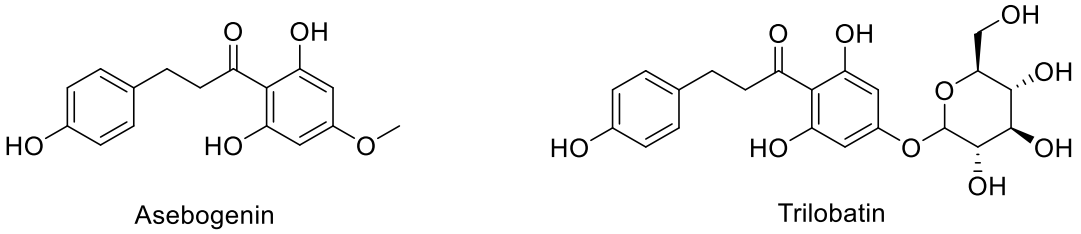
Chapter 1

Introduction

1.1 Introduction

There is no doubt that the pressure from rapid global growth and development has increased the demand for chemicals, in particular fragrances, flavours, pharmaceuticals and agrochemicals.[1,2] The increasing interest in chemical materials has driven researchers to design and develop new strategies based on the use of catalysts for the production of pure specialist compounds with less environmental impact, such as those shown in Scheme 1.1.



Scheme 1.1: Representative examples of natural dihydrochalcone compounds

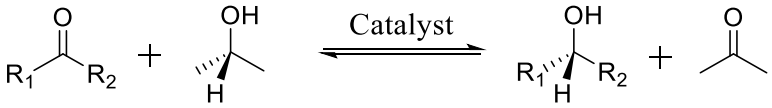
Among the numerous chemical transformations, the hydrogenation of C=C and C=O functional groups are some of the most significant and interesting achievements in both academia and industry. Such transformations have been the subject of interest of many research groups due to the span of their application from fine chemicals to pharmaceuticals.[3–5] Moreover, the chemoselective reduction of a particular group with a minimal effect on another is still a problematic issue in organic synthesis. Hydrogenation can be achieved by three main methods: hydrogenation by metal hydrides, addition of molecular hydrogen mediated by transition metal catalysis and catalytic transfer hydrogenation (TH). Conventionally, metal hydrides such as sodium borohydride or lithium aluminium hydride have been widely used to achieve this reaction.[6] Despite the reliability and robustness of metal hydrides, they generate stoichiometric amounts of waste by-products, which would cause further environmental concern. Also, the separation of such by-products from the reaction medium can be difficult and they generally cannot be recycled. Moreover, the use of metal hydrides often requires special work up. Therefore, they would not be considered sustainable.[7] On the other hand, the addition of atom

economic and sustainable molecular hydrogen in the presence of catalysts can overcome these problems. However, the direct hydrogenation is usually performed under a pressure of hydrogen gas, which requires special handling and equipment. In addition, molecular hydrogen is a highly flammable gas which raises a safety issues of handling and storage.[8]

TH is a convenient and powerful method for hydrogenation, in which a hydrogen source other than hydrogen gas is used. Compared to metal hydrides or direct hydrogen gas reductions, TH simplifies hydrogenation, and is considered less hazardous. Furthermore, the hydrogen sources are usually inexpensive, readily available and easy to handle.[9,10] Therefore, the main goal of this chapter is to give an overview relating to the development of new methods and catalysts in the area of TH of aldehydes and α,β-unsaturated carbonyl compounds.

1.2 Transfer hydrogenation

TH refers to the addition of hydrogen to unsaturated bonds from alternative sources other than dihydrogen in the presence of metal catalysts. Typically, this process involves the transfer of hydrogen from a suitable source (hydrogen donor), with the aid of catalysts, to the unsaturated substrate (hydrogen acceptor) as shown in Scheme 1.2.



Scheme 1.2: Catalytic TH with isopropanol as source of hydrogen

According to Braude and Linstead, the strategies for TH reactions can be classified as follows:

1. Migration of hydrogen which would happen within one molecule (intramolecular).

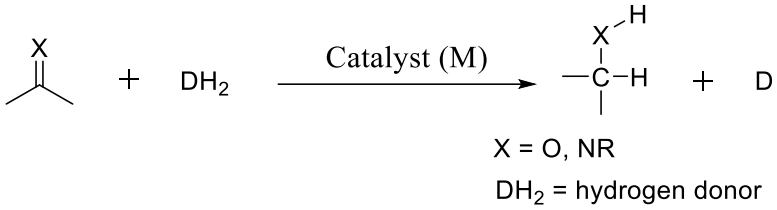
2. Hydrogen disproportionation which involves transfer between similar acceptor and donor units (intermolecular).

3. Transferring hydrogen atoms through a hydrogenation-dehydrogenation process, taking place between dissimilar acceptor and donor units.[11]

In terms of principle, all of these reactions can be carried out either thermally or photochemically, by heterogeneous catalysis, homogeneous catalysis or biological processes.[9] Under mild conditions, only organic compounds with a low oxidation potential can donate hydrogen in a TH reaction, whereas, at high temperature and with the aid of catalysts, many organic species can serve as hydrogen donor. Thus, a wide variety of hydrocarbons, alcohols, acids and hydrides can act as potential hydrogen donors.[8]

1.2.1 Hydrogen donors

The reduction of C=X multiple bonds *via* TH requires a source of hydrogen known as the hydrogen donor, as shown in Scheme 1.3.



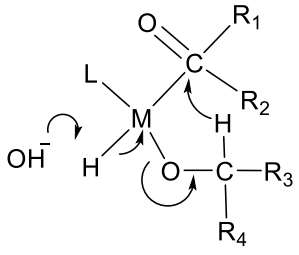
Scheme 1.3: General catalytic TH reaction

Different kinds of compounds such as alcohols, hydrocarbons, cyclic ethers, hydrazine and formic acid have been widely used as hydrogen donors. The more active and commonly used hydrogen donors for such catalytic transformations appear to be formic acid and its salts such as the azeotropic formic acid/trimethylamine mixture (F/T) or alcohols such as isopropanol.[8,12,13] These reagents show excellent performance in the area of TH of carbonyl compounds due to their remarkable ability to proceed under mild reaction conditions, often without the need for inert gas protection. In contrast, these reagents have some disadvantages that influence their role as a hydrogen donor. For example, formic acid is not compatible for use with some catalysts due to its nature of acidity, which may cause a strong interaction with the catalyst and can easily inhibit, deactivate or decompose the catalyst.[13]

The use of alcohols as the hydrogen source can overcome the interaction problems. However, it was found that with the commonly used hydrogen donor alcohols, such as isopropanol, the reduction reaction can be reversible and in order to shift the equilibrium towards the product an excess amount of alcohol would be essential.[13,14] In this thesis, we will show for the first time that methanol can be more efficient than traditional hydrogen donors for the selective reduction of aldehydes and α,β-unsaturated carbonyl compounds under mild conditions.

1.2.2 Promoters

Generally, when alcohols such as isopropanol is used as hydrogen donors in TH reactions, the presence of a base in catalytic amounts is often essential to give the highest levels of catalytic efficiency for the reactions to proceed. Metal alkoxides or hydroxides have played significant roles in the TH of unsaturated bonds.[15,16] These promoters have an advantageous effect on reaction rates by lowering the activation barrier of the hydrogenation step through the generation of a powerful nucleophilic anion. It is believed that the resulting anion is in charge of removing a proton from the reacting complex during the catalytic cycle (Scheme 1.4)[8] and it was found that the formation speed of the nucleophilic alkoxide complex is affected by the type and concentration of the promoter.[17]



Scheme 1.4: Effect of promotor in the TH with isopropanol

For example, Bäckvall and co-workers reported that in the presence of sodium hydroxide as a co-catalyst, the $RuCl_2(PPh_3)_3$ complex catalyses the TH of both aliphatic and aromatic ketones efficiently by the use of *i*PrOH at 82°C. While in the absence of sodium hydroxide no reaction

had been observed mainly because the dissociation of triphenylphosphine was extremely difficult under the same reaction conditions.[16]

1.2.3 Effect of temperature in catalytic TH

It is noted that in most homogeneous catalytic systems temperature has a critical effect on catalytic TH. The benefit of increasing the temperature is to increase the overall rate of the reduction reaction. However, in some cases, raising the temperature could encourage unwanted side reactions such as over-reduction, or result in substrate decomposition. Furthermore, the rate of associated reverse reaction would be also increased. Generally, for the same metal, transferring the hydrogen from a donor to an acceptor with homogeneous catalyst requires a higher temperature than using the heterogeneous ones.[8] Nevertheless, besides the reaction temperature, there are some other factors that could be utilised in TH such as nature of catalyst and type of hydrogen donor and acceptor to successfully increase the reaction rate at a lower temperature.[8,9]

1.2.4 Effect of solvent in catalytic TH

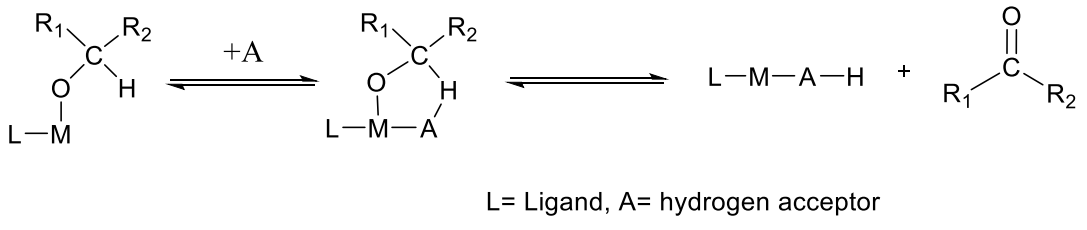
One of the significant factors that affect the catalytic activity in TH reductions is the right choice of solvent. The influence of solvent in TH in general, except when the solvent also acts as the hydrogen donor, is linked to its ability to dissolve the reaction species. In preliminary studies carried out to evaluate the solvent effects, it was found that reaction times are significantly affected.[9,18] Generally, the coordination of the soluble catalyst could be either to the ligand or to the solvent. Sometimes, the solvent displaces the ligand resulting in new more or less active complexes. In case of reactivity, the solvent coordination to the metal may change the electron density surrounding the metal atom which changes the complexation ability towards the reactions, for example, oxidative addition. In solution, the metal catalyst becomes active when one or more ligands dissociate leaving the central metal atom coordinatively

unsaturated, which eventually facilitates the subsequent step. The catalysts activity could be reduced or even completely lost if the binding link between catalyst and solvent is more powerful than with the hydrogen donor or acceptor. Also, the catalysts activity could be completely destroyed if the solvent pushes the ligand from the central metal without dissociation. So, the best solvent for TH would be the one that can dissociate from the catalyst, and have a weaker binding ability with the metal centre than the hydrogen donors and acceptors.[8]

1.2.5 Mechanism of catalytic TH

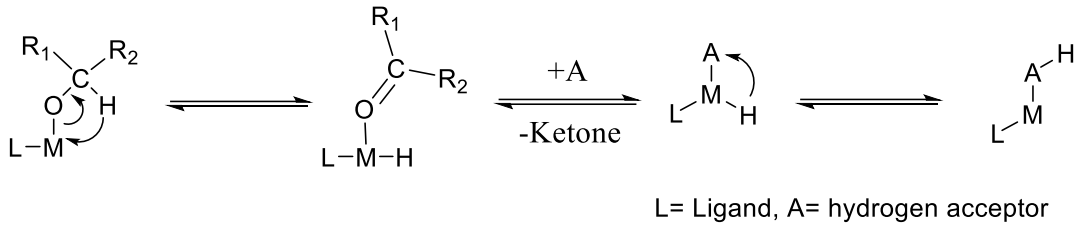
The TH mechanism can be classified according to what was reviewed by Bäckvall *et al.* into two general mechanisms, the direct hydrogen transfer (a concerted process), or the hydridic route (a multi-step process) which are exemplified by Schemes 1.5a and b.[19]

The direct hydrogen transfer involves transferring the hydrogen to the substrate without the involvement of metal hydride intermediates by forming a six membered transition state, in which the metal is attached to the donor and acceptor and they are held by the catalyst together in close proximity. This mechanism possibly occurs through the concerted formation of a cyclic ring transition state similar to the one proposed for the Meerwein–Ponndorf–Verley reduction. So here the metal is playing a role of providing the reactant with the right direction making the hydride transfer feasible.[13,20]



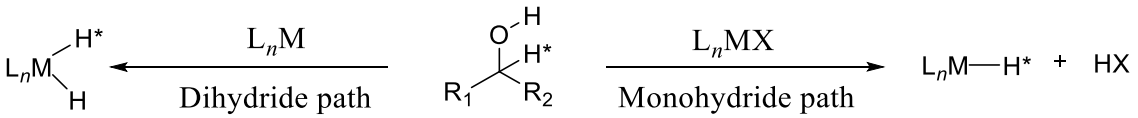
Scheme 1.5a: Direct hydrogen route for TH

The second type of TH mechanism is the hydridic path which operates *via* the formation of 4 membered transition state. This route involves an interaction between the catalyst and the hydrogen donor followed by transferring the hydride from the metal to the acceptor (substrate) without the interaction with both, the hydrogen donor and acceptor, at the same stage of the mechanism.



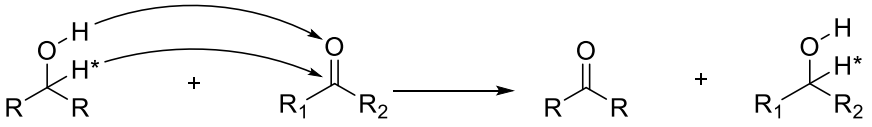
Scheme 1.5b: Hydridic route for TH

For the hydridic route, Bäckvall and co-workers observed that TH reaction proceeds via two principally different pathways depending on the type of the formed metal hydride, and these paths are monohydride and dihydride pathways (Scheme 1.6).



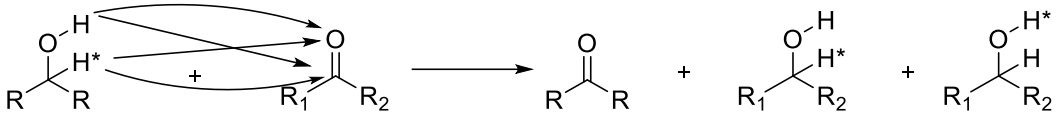
Scheme 1.6: Hydridic route pathways for TH

In the monohydride route both O-H and C-H hydrogens of the donor are selectively transferred to the keto oxygen and carbonyl carbon of the acceptor without changing their identity. The reason behind this order is that the metal hydride is formed only from the C-H of the donor while the O-H hydrogen of the donor transferred as proton to the acceptor as shown in Scheme 1.7.[21]



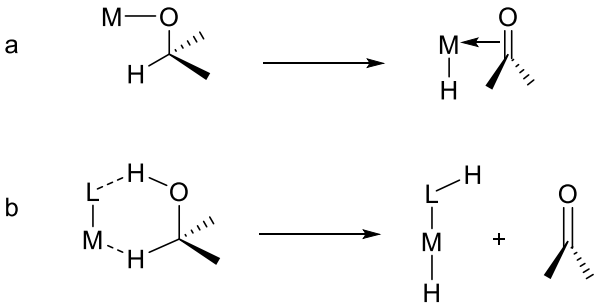
Scheme 1.7: Monohydride pathway for TH of ketones

Contrarily, in the dihydride pathway the hydrogens of the donor lose their identity when they transferred to the acceptor, *i.e.* both O-H and C-H hydrogen become equivalent when they transferred to the metal and give the hydride as shown in Scheme 1.8.[22]



Scheme 1.8: Dihydride pathway for TH of ketones

Concerning the monohydride pathway, another classification arises based on the formation of the metal monohydride, defined as the inner sphere and outer sphere mechanisms. In the inner sphere mechanism, the hydride transfer proceeds through the formation of the metal monohydride from the hydrogen donor by a transition metal alkoxide followed by β-elimination to give the M–H. The outer sphere mechanism proceeds via a concerted pathway in which the α-C-H transferred to the metal and the O-H to the ligand without coordination to the metal (Scheme 1.9).



Scheme 1.9: Monohydride mechanism involving inner sphere (a) and outer sphere pathway (b)

1.3 Selective transfer hydrogenation of carbonyl compounds

Aldehydes are the simplest example of carbonyl compounds which consist of a carbon atom attached by a double bond to an oxygen and to a hydrogen by a single bond. These compounds

represent significant building blocks in organic synthesis due to their ability to function as a nucleophile and an electrophile.

The word “aldehyde” was introduced by Justin von Liebig in the early 19th century, using the contraction of the Latin words “alcohol deprived of hydrogen” or “alcohol dehydrogenatus”.[23] The general formula for aldehydes is RCHO, R = aliphatic or aromatic group. By comparing the carbonyl group (C=O) in aldehydes with the C=C double bound in alkenes, we realise that they have different properties and reactivity. For example, the reactivity of C=O groups towards nucleophilic attack is higher than C=C bonds due to the electronegativity of the oxygen atom, which results in a decrease in the length of C=O bond to 1.21 Å (Figure 1) and causes the higher polarity of these compounds. As a consequence of this polarisation, aldehydes possess higher boiling points and solubilities than the hydrocarbons of the same molecular weight.[24]

Figure 1: The bond distance values of the C=O and C=C bounds

Basically, there are two types of reactions that aldehydes can undergo, one of which relates to the carbonyl group and the other belongs to the alpha carbon (Figure 2). Here, we focus on the selective reduction reaction of the carbonyl group.

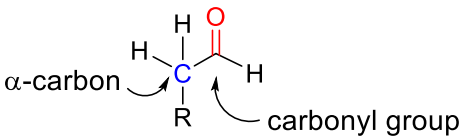
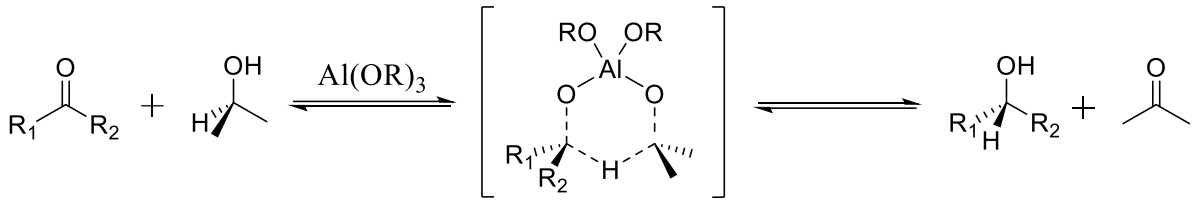


Figure 2: Examples of reaction centres of aldehydes

Carbonyl reduction to the corresponding alcohol represents one of the most fundamental transformations in both the pharmaceutical and chemical industries.[13,25] The first examples of such transformation date back to more than a century as Levene and Taylor reported the

reduction of aldehydes with the use of zinc dust in glacial acetic acid solution or by the use of sodium amalgam[26]. In the mid-1920s, independently Meerwein, Ponndorf and Verley reported the first chemoselective example of carbonyl reduction using aluminium alkoxides with secondary alcohols as a source of hydrogen to produce the corresponding alcohols. The reduction involves a direct path of hydrogen transfer *via* the formation of a six-membered cyclic transition state, in which the metal is coordinated to both alcohol and ketone (Scheme 1.10).[14,27–29]

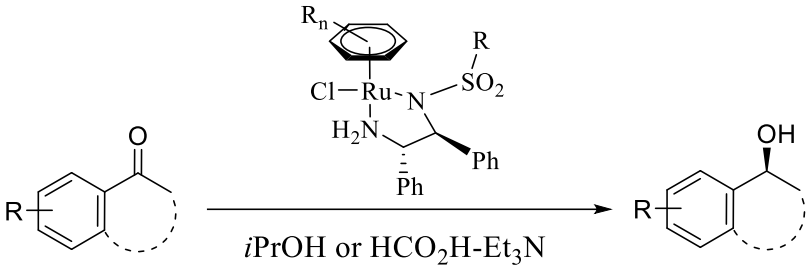


Scheme 1.10: The hydrogen transfer *via* a cyclic six-membered transition state pathway

After this discovery, many attempts have been made in this area to enable fast, selective and productive TH. In 1930, di-borane was introduced by Schlesinger as a reducing agent for the carbonyl reduction under mild conditions.[30] However, the rarity of di-borane at that time had negative consequences, leading to the restriction of its development. Later in 1942 and 1945, both sodium borohydride and lithium aluminium hydride were discovered, and made radical changes in the field of carbonyl reduction.[30]

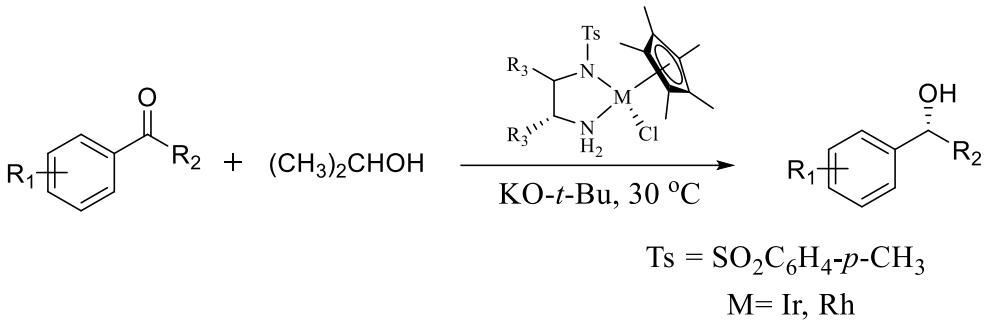
A significant advance in TH of carbonyl compounds was the discovery by Henbest, Mitchell, and co-workers in the 1960s, showing that transition metals such as iridium can catalyse carbonyl reductions to the corresponding alcohol in the presence of isopropanol.[31] Another important contribution to the TH of carbonyls was provided in 1975 by Sasson and Blum, reporting the use of dichlorotris(triphenylphosphine)ruthenium [$RuCl_2(PPh_3)_3$] for the reduction of carbonyls in α,β-unsaturated compounds with isopropanol at high temperature.[18] In the same context, Chowdhury and Bäckvall after two decades were able to accelerate

$[RuCl_2(PPh_3)_3]$ reactivity towards the reduction of aliphatic and aromatic carbonyls by using catalytic amounts of base that act as a co-catalyst. The role of the base is to form the active ruthenium dihydride through the displacement of the chloride followed by β-elimination.[10,16] The second milestone for carbonyl TH was provided by Noyori and co-workers in 1995. The ruthenium complexes (Ru-TsDPEN) introduced by this group were capable of the asymmetric reduction of various ketones and imines as shown in Scheme 1.11.



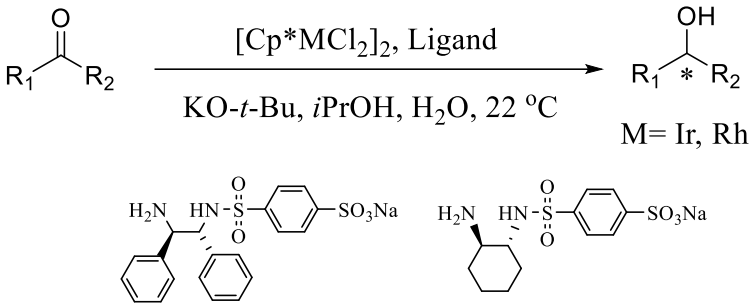
Scheme1.11: Noyori's TH of cyclic and acyclic ketones

The contribution of Noyori, who was awarded a Nobel Prize in 2001, has led to great progress in TH, allowing the use of various types of hydrogen donors, associated with the operational simplicity and the high selectivity of the catalyst.[32] Such discovery has inspired many researchers to develop various combinations of ligands using other metal complexes such as half-sandwich rhodium and iridium compounds. For example, Ikaria and co-worker disclosed new chiral complexes of pentamethylcyclopentadienyl (Cp*) iridium and rhodium with diamine ligands. These complexes exhibited excellent activity and selectivity to catalyse the asymmetric transfer hydrogenation (ATH) of carbonyl compounds (Scheme 1.12).[33]



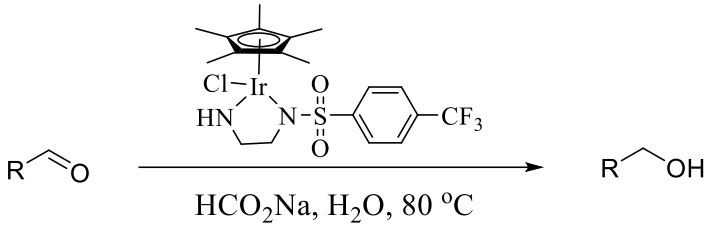
Scheme1.12: Examples for A TH with Chiral Rh or Ir Cp* complexes

Similarly Williams *et al.* used the Cp* iridium and rhodium complexes with amino sulfonate ligands shown in Scheme 1.13 to form a water-soluble chiral catalyst that is efficient for the ATH of aromatic ketones. The best results for this catalyst are obtained when the reaction mixture contains 15 to 34% water.[34]



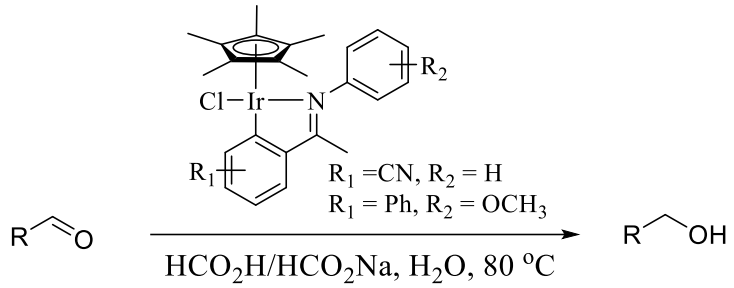
Scheme1.13: Examples of ATH with chiral Cp* Rh or Ir complexes

Wu of our group reported highly selective TH of various aliphatic and aromatic aldehydes in aqueous phase, using Cp*Ir with monotosylated ethylenediamine ligands. The system shows excellent results for the selective reduction of aldehydes in the presence of other sensitive functional groups such as ketones and alkenes (Scheme 1.14).[35]



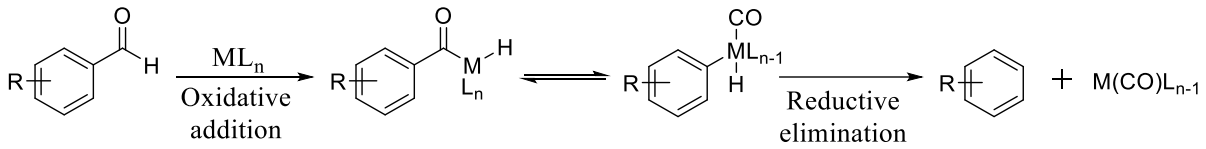
Scheme1.14: Examples for TH with Cp* Ir monotosylated ethylenediamine complexes

Recently, our group demonstrated that iridacyle complexes are efficient for the TH of carbonyl compounds under aqueous conditions. A wide range of aldehydes and α,β-unsaturated aldehydes have been reduced with high activity and chemoselectivity affording alcohols and allylic alcohols under acidic conditions (Scheme 1.15)[36,37]



Scheme1.15: Examples for TH with iridacyle complexes

Despite the fact that over several decades the TH of carbonyl compounds has been well-addressed, there are still some areas that need improvement. In particular, low-cost methanol has been rarely used as a hydrogen donor. Previously, it was reported that TH with methanol in general is limited to the reduction of ketones rather than aldehydes for two reasons. Firstly, under basic conditions required for the TH, the aldehyde undergoes deprotonation of CH group next to the carbonyl that resulted in the formation of aldol products instead of the simple reduction. Secondly, the aldehyde can undergo decarbonylation, especially with Ir and Rh based catalysts, which leads to the transferring of the carbonyl group from aldehyde to the metal and poison the catalyst (Scheme1.16).[38,39] Therefore, secondary alcohols such as 2-propanol have been more extensively used for the reduction of aldehydes, because this decarbonylation process does not take place.

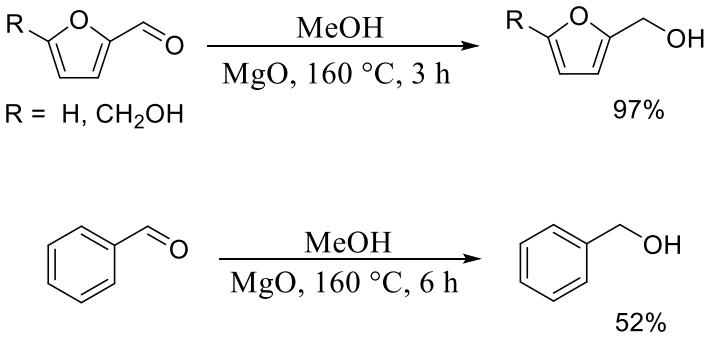


Scheme 1.16: Catalyst poison *via* carbonyl transfer from aldehyde to the metal

In recent years, the field of homogeneous catalysis has witnessed major advances in the discovery of many active catalysts that has allowed TH of aldehydes with various alcohols under mild conditions. Nevertheless, only a few examples have been reported for the use of methanol for the selective TH of aldehydes.

In an earlier study conducted by Maitlis *et al.*, it was reported that methanol could be used as a hydrogen donor for the reduction of carbonyl compounds, especially the reduction of ketones. Rh, Ir, Ru, and Os complexes were applied for the transfer reduction with methanol as a donor, and it was found that among all the complexes, $RuCl_2(PPh_3)_3$ is the most effective complex for the reduction. However, this complex was much more efficient in case of ketone reduction than aldehydes.[40]

Pasini *et al.* have also studied the use of methanol as a source of hydrogen for the reduction of 5-hydroxymethylfurfural using magnesium oxide at 160 ºC. This system has been found to be highly effective in case of furfural. However, when they switched the substrate to benzaldehyde, the reaction required a longer reaction time than that reported with furfural (Scheme 1.17).[41]

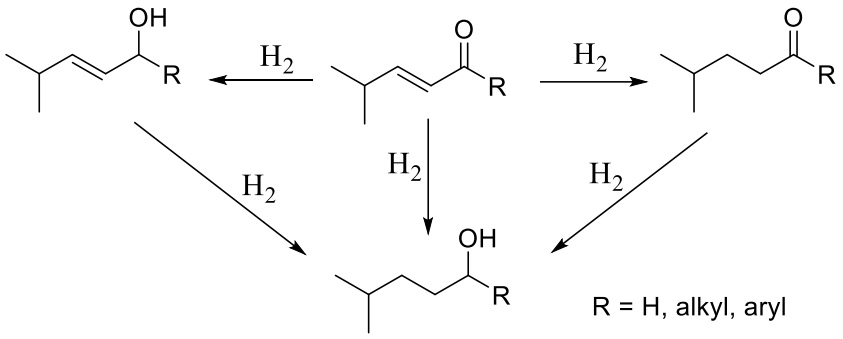


Scheme 1.17: Examples of reduction of aldehydes with MgO in methanol

1.4 Selective transfer hydrogenation of α,β-unsaturated carbonyl compounds

α,β-Unsaturated carbonyl compounds are the core of many biologically interesting compounds containing conjugated carbon-carbon and carbon-oxygen double bonds. These compounds are attractive substances used industrially as starting materials of a large number of compounds, including plastics and resins, pesticides, dyes, pharmaceuticals and fine chemicals, particularly in the field of flavour and fragrance chemistry.[42–44]

The importance of α,β-unsaturated carbonyl compounds is due to the wide range of applications of these compounds. Various attractive products could be obtained from the selective or complete reduction of one or both of the conjugated double bonds as shown in Scheme 1.18.

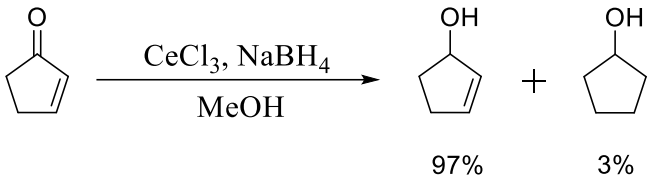


Scheme 1.18: Reaction pathways in the hydrogenation of α,β-unsaturated carbonyl compounds

1.4.1 Selective transfer hydrogenation of α,β-unsaturated ketones

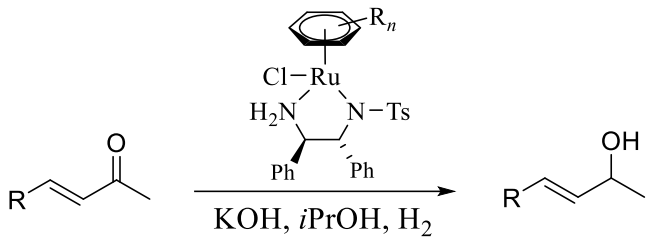
As we mentioned above, the chemoselective TH of α,β-unsaturated ketones can occur either on the carbonyl group which is known as 1,2-reduction to give the allylic alcohol product, or on the olefinic double bond known as 1,4-reduction affording the saturated ketone product. The reduction of the carbonyl moiety is more developed when compared with the olefinic reduction, which remains limited and a challenging problem in organic synthesis.[45] One of the most popular methods used for the selective reduction of the unsaturated ketones to the allylic alcohol is the use of $NaBH_4$ with cerium chloride in methanol. The presence of cerium chloride

has shown high selectivity for the reduction of the carbonyl group over the conjugated C=C double bond (Scheme 1.19).[46]



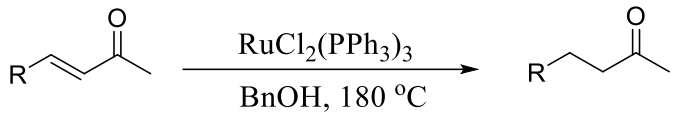
Scheme 1.19: Examples of reduction of α,β-unsaturated ketones

Progress has also been made for the selective reduction of carbonyls using different types of metal complexes. The bifunctional ruthenium complex that was described by Noyori *et al.*, for example, was found to be highly chemoselective for the hydrogenation of α,β-unsaturated ketones to afford the allylic alcohol in almost quantitative yields (Scheme 1.20).[47,48]



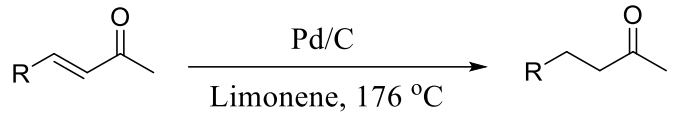
Scheme 1.20: Reduction of α,β-unsaturated ketones with a Noyori catalyst

However, the selective 1,4-reduction of α,β-unsaturated carbonyl ketones has not been developed so much, mainly because most of the methods that are used for the reduction suffer from strict reaction conditions, such as high temperatures, handling of reagents and long reaction times.[49] For example, the $RuCl_2(PPh_3)_3$ catalyst, which was reported by Sasson and co-workers for TH of α,β-unsaturated ketones, was found to be highly selective towards the unsaturated bond arising from the use of different alcohols. However, the optimal reduction conditions required high temperatures (up to 180 ºC) with benzyl alcohol as the best hydrogen donor (Scheme 1.21).[18]



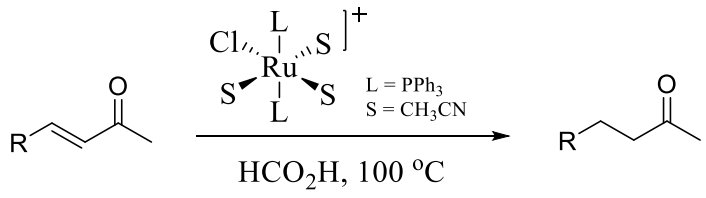
Scheme 1.21: Reduction of α,β-unsaturated ketones with a ruthenium catalyst

Palladium supported on carbon reported by Oliveira *et al.* was also very active for the TH of the unsaturated bond of α,β-unsaturated ketones. Using limonene as a hydrogen donor the selectivity of the catalyst towards the saturated ketone product is 100%. But again high temperatures of ca 176 °C are an essential requirement for complete reaction (Scheme 1.22).[49]



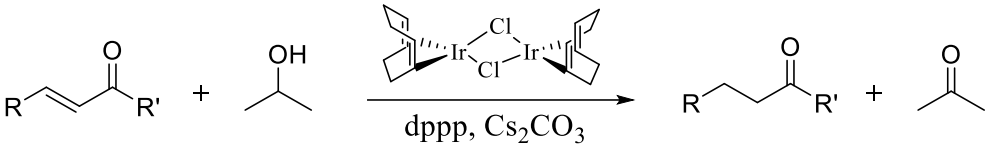
Scheme 1.22: Reduction of α,β-unsaturated ketones with a palladium catalyst

Recently, the remarkable progress in the field of catalytic TH for environmentally "green" processes revealed that the reduction of unsaturated ketones can be easily achieved with the use of organic hydrogen donors such as formic acid and common alcohols under milder reaction conditions. For example, Naskar and Bhattacharjee explored the catalytic activity of a cationic Ru complex for the selective reduction of the C=C double bond in α,β-unsaturated ketones. Although the reduction was performed using formic acid as a hydrogen source under solvent-free conditions affording the saturated ketone in good yields, a prolonged reaction time (6 h) was essential for the reaction to complete. (Scheme 1.23).[50]



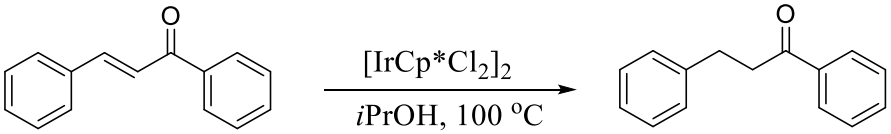
Scheme 1.23: Reduction of α,β-unsaturated ketones with formic acid

Ishii and co-workers reported the use of $[Ir(cod)Cl]_2$ complex with 2-propanol for efficient selective TH of the α,β-unsaturated ketones to the saturated ketones under mild condition. The reaction was successfully achieved in the presence of Cs_2CO_3 within 4 h time as shown in Scheme 1.24.[51]



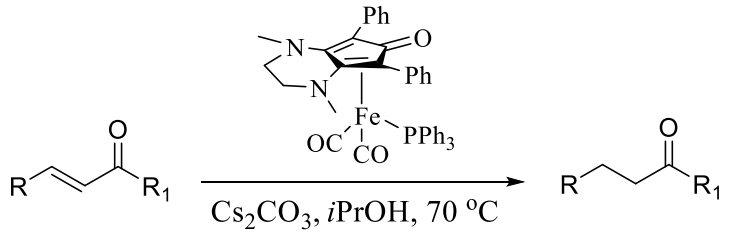
Scheme 1.24: Reduction of α,β-unsaturated ketones with 2-propanol

Reported by Chen *et al.*, the $[IrCp^*Cl_2]_2$ complex showed excellent activity with the use of isopropanol as a hydrogen donor for a diverse range of substituted α,β-unsaturated carbonyl compounds, providing the saturated ketones is up to 92% yield in 5 h. However, when they switched the solvent to methanol the yield dropped to 31% (Scheme 1.25).[52]



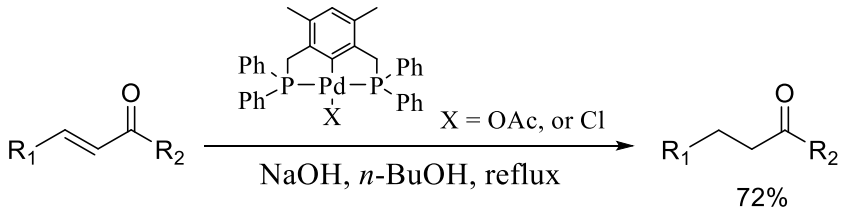
Scheme 1.25: Reduction of α,β-unsaturated ketones with isopropanol

Lator *et al.* disclosed the use of an iron catalyst with isopropanol as a source of hydrogen to reduce the olefinic bond of a broad range of α,β-unsaturated ketones, obtaining the desired product in good to excellent yields. Nevertheless, this system requires a quite long time (16 h) to complete the reaction (Scheme 1.26).[53]



Scheme 1.26: Reduction of α,β-unsaturated ketones with isopropanol

As we have already noted, methanol is an eco-friendly, cost-effective and easily available source of hydrogen from many viewpoints. However, only a few reports of its use in the reduction of unsaturated ketones were reported. This lack of interest in methanol may be due to the lack of catalyst activity towards the dehydrogenation of methanol or, the use of methanol requires harsher reaction conditions. For example, Ding *et al.* explored a pincer Pd complex towards the selective reduction of unsaturated ketones. The complex showed good activity with the use of *n*-BuOH as a hydrogen source; however when they used methanol under the same conditions, the catalyst became less effective and resulted in a lower yields of only 9% (Scheme 1.27).[54]



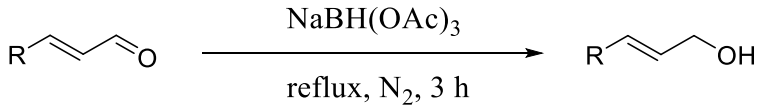
Scheme 1.27: Reduction of α,β-unsaturated ketones with *n*-BuOH

1.4.2 Transfer hydrogenation of α,β-unsaturated aldehydes

α,β-Unsaturated aldehydes and their chemoselective reduction products (unsaturated alcohol, saturated aldehyde and saturated alcohol) are very important in pharmaceutical and fine chemical production. This is due to their wide range of applications in the synthesis of flavours, fragrances and polymers.[55,56] In general, and for the production of small-scale compounds, the selective reduction of α,β-unsaturated aldehydes is usually achieved using stoichiometric

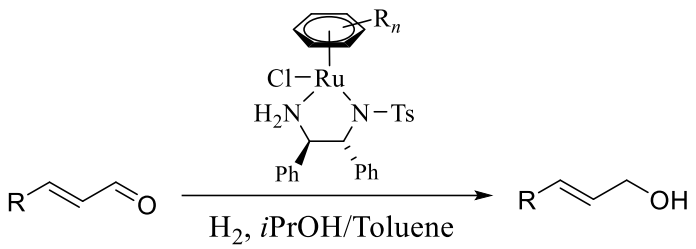
amounts of metal hydrides such as $LiAlH_4$. Depending on reaction conditions, the reduction of α,β-unsaturated aldehydes with these types of reducing agents can give either saturated or unsaturated alcohols or can afford a mixture of both. For example, in the reduction of cinnamaldehyde, when the reagent is added to a solution of the substrate, the resulting product would be the allylic alcohol, while the addition of the substrate to a solution of the reducing reagent gave the 3-phenyl-1-propanol.[57]

The reduction of α,β-unsaturated aldehydes is one of the topics that is most widely investigated, especially the selective reduction of the aldehyde to produce unsaturated alcohols or the reduction of the olefin to afford the saturated aldehydes. For example, the selective reduction of unsaturated aldehydes to allylic alcohols have been achieved by metal hydrides such as sodium triacetoxyborohydride. This metal hydride that is prepared by reacting sodium borohydride with glacial acetic acid was found to be highly efficient for the selective reduction of aldehydes with good to excellent yields (Scheme 1.28).[58]



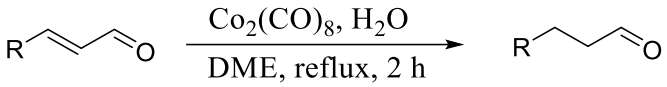
Scheme 1.28: Selective reduction of α,β-unsaturated aldehydes with metal hydrides

Another method that has been developed for the conversion of unsaturated aldehydes into allylic alcohols is the hydrogenation reaction with transition metals complexes. Noyori's ruthenium catalyst is a remarkable example that exhibits a very high selectivity for the reduction of both aliphatic and aromatic unsaturated aldehydes into allylic alcohols in high yields (Scheme 1.29).[48]



Scheme 1.29: Selective reduction of α,β-unsaturated aldehydes with a Noyori Ru catalyst

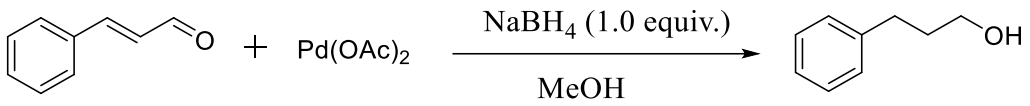
In contrast, the selective reduction of α,β-unsaturated aldehydes to saturated aldehydes has been quite challenging and remain unexplored. Compared with the methods stated above, the selective reduction of the olefinic bond in α,β-unsaturated aldehydes is usually achieved through the use of unusual reagents.[59]An *et al.* reported the application of dicobalt octacarbonyl for the selective reduction of the olefinic bond of α,β-unsaturated aldehydes. The selective reduction of the C=C double bond was successfully conducted in the presence of water to afford the saturated aldehyde in good to excellent yield (Scheme 1.30).[60]



Scheme 1.30: Selective reduction of α,β-unsaturated aldehydes with dicobalt octacarbonyl

The conversion of α,β-unsaturated aldehydes into saturated alcohols is also challenging and difficult to achieve by heterogeneous or homogeneous catalysis. This is because the reduction of the former is readily occurring by the use of H_2 with metal catalysts, while the carbonyl is generally hydrogenated by hydride source. Therefore, the reduction of unsaturated aldehydes to the corresponding saturated alcohols may require a special reducing system. As an example, De Castro *et al.* reported that $Pd(OAc)_2$ in the presence of $NaBH_4$ can successfully catalyse the reduction of α,β-unsaturated aldehydes at room temperature, producing the corresponding fully saturated aldehydes in good to excellent yields (Scheme 1.31). $NaBH_4$ was found to be essential

not only for the reduction of the carbonyl group but also to reduce the $Pd(OAc)_2$ to Pd (0) which is then used to catalyse the reduction of the C=C double bond.[61]

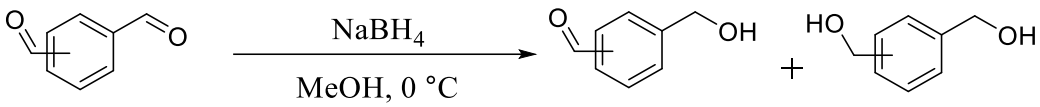


Scheme 1.31: Hydrogenation of α,β-unsaturated aldehydes with $Pd(OAc)_2$

1.5 Selective reduction of di-aldehydes

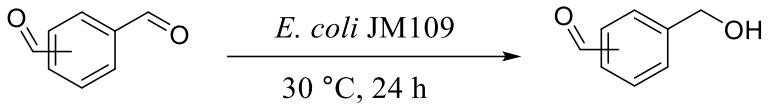
Selective hydrogenation of aldehydes in the presence of other sensitive groups are among some of the most important transformations for the production of alcohols, which are a valuable raw material in the pharmaceutical, flavour, fragrance, and agrochemical industries.[62] Significant work using different metal complexes, such as iridium,[35] iron[63] and molybdenum,[64] have been published for the selective reduction of aldehydes over ketones and other reducible groups. These complexes showed high chemoselectivity for the reduction of aldehydes, allowing the production of corresponding alcohols in high yields. However, there are some groups that can interfere with the reaction, for example, the presence of additional aldehyde groups (di-aldehyde compounds) will make these metal complexes less selective.

The selective hydrogenation of di-aldehydes into hydroxymethyl aldehydes is another difficult task in organic synthesis, and it has remained less developed. Generally, the production of hydroxymethyl aldehydes can be achieved either by the selective oxidation of dialcohols which are generally more expensive substrates, or by the selective reduction of dialdehydes.[65] The selective reduction of dialdehydes are usually carried out with stoichiometric amounts of metal hydrides such as sodium borohydride. Nevertheless, the use of metal hydrides, which is always accompanied with stoichiometric amounts of undesired waste products, can result in poor selectivity ending with the formation of saturated di alcohols (Scheme 1.32).[66,67]



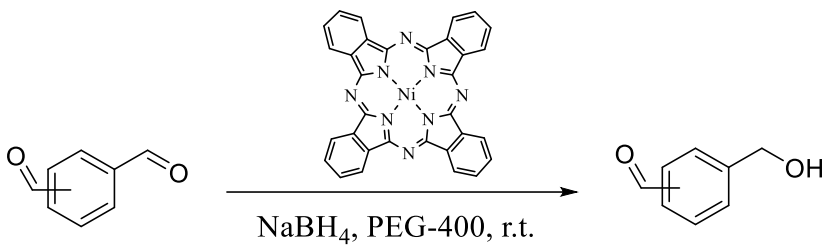
Scheme 1.32: Examples of selective reduction of dialdehydes

Lately, there has been some research focused on developing new methods that allow selective reduction of dialdehydes to the corresponding alcohols. For example, Sello and co-workers showed a new enzymatic method for the selective reduction of dialdehydes. The *E. coli* strain (JM109) performed a high selective bioconversion of dialdehydes into their hydroxymethyl aldehydes (Scheme 1.33). However, the performance of this strain is affected by forming an unidentified side product when both aldehyde groups are in *ortho* position to each other.[68]



Scheme 1.33: Examples of selective reduction of di-aldehydes

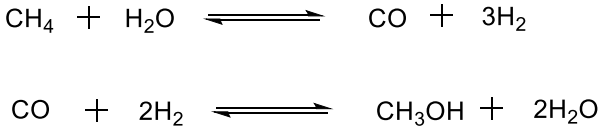
Verma *et al.* demonstrated that the abundantly available and cost-effective nickel is capable of the selective reduction of dialdehydes at room temperature. Nickel phthalocyanine along with polyethylene glycol-400 was found to be highly chemo- and region-selective for the reduction of aldehydes utilising sodium borohydride as a hydrogen source with moderate to good yields under mild conditions (Scheme 1.34). Nevertheless, the catalyst suffers from the lack of chemo-selectivity when the *ortho* di-aldehyde substrate is used, affording the fully reduced alcohol product.[25]



Scheme 1.34: Selective reduction of daldehydes with nickel complex

1.6 Methanol as hydrogen source

Methanol or methyl alcohol is the simplest aliphatic alcohol consisting of a methyl group attached to a hydroxyl group. At room temperature methanol is a colourless, polar, volatile and flammable liquid, with a distinctive odour similar to ethanol. The history of methanol dates back to the ancient Egyptians as they used it in their embalming process.[69] The first commercial production of methanol is from the destructive distillation (pyrolysis) of wood. Although the production of pure methanol was reported by Robert Boyle in 1661, the elemental structure of methanol remained unknown until the beginning of the 1830s. After the successful commercialisation of methanol production, the term "methyl" was introduced into chemistry by Jean-Baptiste Dumas and Eugene Peligot who successfully reported the elemental composition for methanol in 1835. Then, methanol production prevailed for about one century until the Badische Anilin und Soda Fabrik (BASF) commercialized the first synthetic manufacture of methanol plant in 1923. Since then, methanol production has undergone drastic improvements and has now become important worldwide with total production exceeding more than 85 million tons in 2016.[69–72] Nowadays, methanol can be produced from many different carbon-containing sources such as CO, natural gas, coal and biomass. Moreover, there are some other alternative sources that can also produce methanol but with lower yields.[73] The steam reforming of natural gas to eventually produce methanol is shown in Scheme 1.35.



Scheme 1.35: Methanol production from steam reforming of methane

Currently, about 35 percent of methanol is used as a raw material for the production of formaldehyde and as a C1 building block in the petrochemical industry. The remaining percentage of methanol is used as a general solvent in organic synthesis, fuel or fuel additives,

antifreeze and rocket fuels. Moreover, methanol can be used for synthetic resins, dyestuffs, perfumes, pharmaceuticals and other chemicals.[70,72,74]

The great interest in the use of methanol for the fuel cell application (hydrogen precursor) is due to the high hydrogen content of methanol (about 12.5%). Moreover, the complete conversion of methanol to hydrogen and carbon monoxide occurs under moderate conditions about (150-350 ºC) which is lower than that needed for other fuels (>500 ºC). This is due to the fact that methanol has only one carbon atom, which means no additional C-C bond cleavage is required.[75]

The main role of methanol in most chemical reactions would be as a solvent. On the other hand, methanol can also serve as a useful precursor for hydrogen and carbon oxide or for both. From a thermodynamic point of view, methanol conversion to hydrogen and carbon monoxide is unfavourable. Thus, to facilitate such types of transformations the presence of some organic chemicals that can accept the hydrogen is desirable.[40] According to the general observation of the reported oxidation potentials and apart from other properties, secondary alcohols are more favourable to give off hydrogen than primary alcohols and isopropanol is usually the best choice for hydrogenation reactions.[76] This was confirmed by Imai *et al.* in an earlier study for the reduction of cycloheptene with different types of alcohols. The study showed that methanol was slower and much less effective as a hydrogen donor than 2-propanol with a difference in their rates exceeding 1000 times, under the same reaction conditions.[20,40,76]

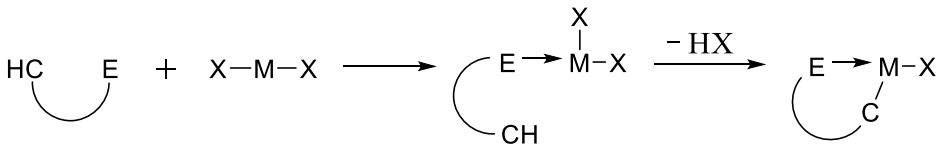
Notably, methanol had been used as an alternative source to the molecular hydrogen for the reduction of a variety of functional groups, such as alkynes,[77,78] alkenes,[79,80] carbonyl[18,81] and nitro.[82,83] The reduction of alkyne, alkene and nitro compounds with methanol as the source of hydrogen and solvent are beyond the scope of this thesis. Thus, only the reduction of carbonyl compounds will be highlighted here. The homogeneous catalytic dehydrogenation of primary and secondary alcohol except for methanol have been investigated thermally and

photochemically. The earliest photochemical studies by Ciamician and Silber showed that ethyl or isopropyl alcohols could be used successfully as a hydrogen donor for the reduction of benzoquinone to the corresponding quinol. However, the application of methanol in transfer hydrogenation was hardly investigated.[84] Braude and Linstead have studied the reaction between benzoquinone and methanol and they estimated the amount of accompanying energy based on the bond and resonance energies to be -5 kcal.[11] Shinoda *et al.* reported the first example of methanol thermal dehydrogenation under homogeneous catalysis. $[Ru_2(OAc)_4Cl(PR_3)_3]$ complex was used under mild conditions to dehydrogenate methanol into formaldehyde evolving the dihydrogen as a gas.[85] In the same year, Smith and Maitlis reported the use of methanol as a hydrogen donor with a diverse of precious metals for the reduction of carbonyl compounds to the corresponding alcohols. However, their method suffered from low yield in case of aldehydes.[40] Hazarika *et al.* reported an aqueous reduction of C=C double bond and carbonyl compounds with the use of aluminium powder and $NiCl_2$ in THF. Their system successfully reduces the target groups in good yields. But when they switched the solvent to methanol the catalytic performance was much lower and resulted in poor selectivity towards the formation of alcohol, reaching 40 percent for ketones and 80 percent in case of aldehydes.[86] Recently, Crabtree *et al.* reported a series of homogeneous iridium complexes prepared from $[Cp^*IrCl_2]_2$ and N-heterocyclic carbene ligands, for the TH of carbonyl with methanol under mild basic conditions. Several aromatic ketones were smoothly reduced to alcohols in good yields; however, the reduction of acetophenones gave poor yields of the corresponding 1-phenylethanols due to the methylation of α-CH_3 group.[81]

Despite the fact that there are some examples for the TH hydrogenation of ketones in the literature, it is noteworthy that no single catalyst has been reported for the use of methanol to hydrogenate aldehydes efficiently to the corresponding alcohol under mild reaction conditions.

1.7 Cyclometalated metal complexes

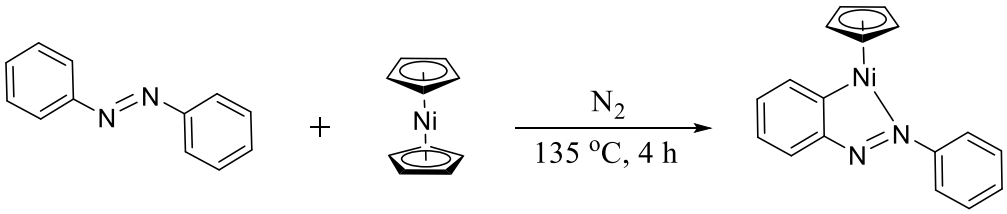
The term cyclometalation was first introduced in 1973 by Trofimenko to describe the formation of a chelate ring containing at least one metal-carbon bond, which is also stabilised by one or more heteroatom donors (such as N, C, O, P) as shown in Scheme 1.36.[87,88] Typically, this reaction involves two sequential steps, starting with the metal coordination with the donor group E, followed by intramolecular activation of the CH bond. The donor E assists the process leading to the metalacycle.



X= Leaving group, M= Metal ion, E= Donor group,
HC= Cyclometalating group

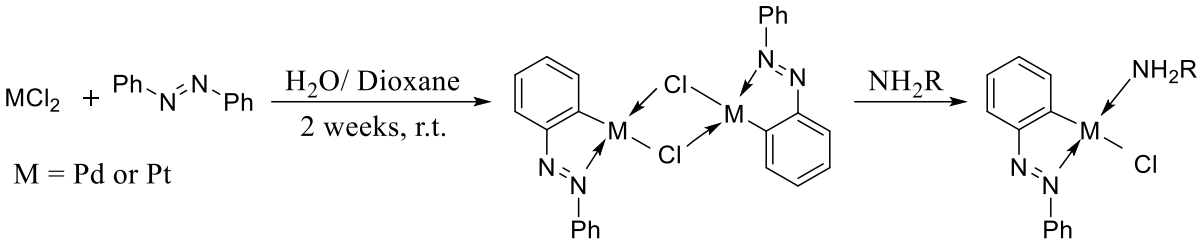
Scheme 1.36: General scheme for cyclometalation reaction

The first example of cyclometalated complexes was prepared in the early 1960s by Kleiman from the reaction of nickelocene and azobenzene (Scheme 1.37)[89].



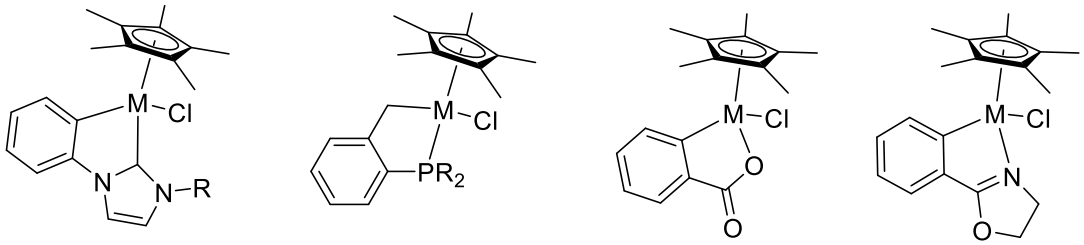
Scheme 1.37: First example of the synthesis of a cyclometalated complex

Later, in 1965 Cope and Siekman reported the synthesis of Pd and Pt dimer complexes. Using a dioxane/water mixture at ambient temperature, they reacted potassium tetrachloroplatinate(II) or palladium(II) dichloride with azobenzene over two weeks to obtain about 48% of the dimer product as shown in Scheme 1.38.[90]



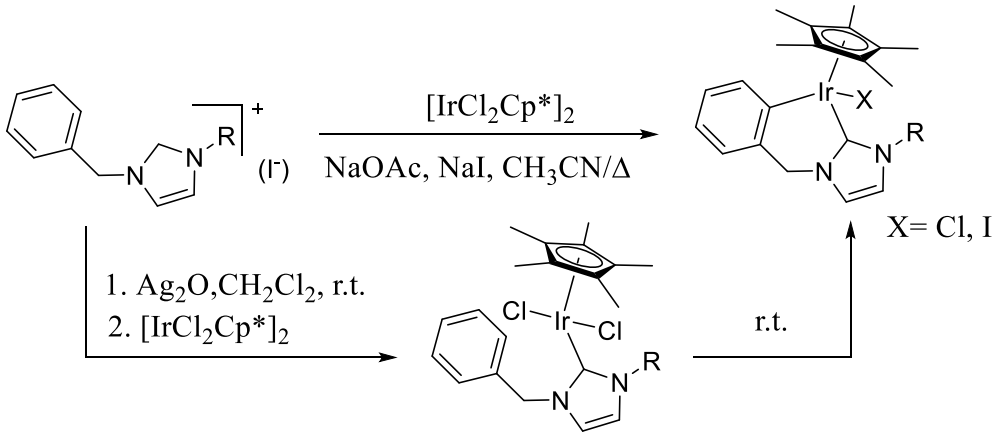
Scheme 1.38: Synthesis of Pd and Pt dimer complexes

Cyclometalated complexes can be classified depending on the type of the donor atom (C, P, O, N). Thus, for half-sandwich complexes there would be four types of metalacycle: [Cp*M(C^C)Cl], [Cp*M(C^P)Cl], [Cp*M(C^O)Cl] and [Cp*M(C^N)Cl] as shown in scheme 1.39.[88]



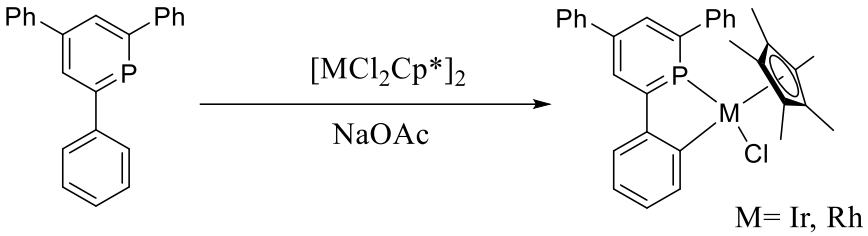
Scheme 1.39: Types of donor classification of half-sandwich complexes

Peris group reported the [Cp*M(C^C)Cl] complexes and their catalytic applications by reacting $[IrCl_2Cp^*]_2$ with the imidazolium salts under basic conditions of sodium acetate (Scheme 1.40).[91]



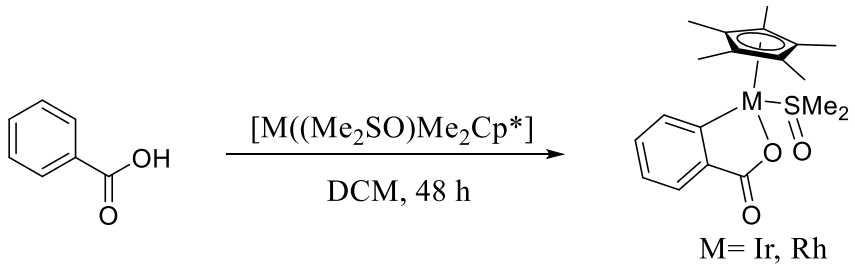
Scheme 1.40: The formation of C^C cyclometalated half-sandwich complexes

Muller *et al.* demonstrated the use of phosphorus for the formation of a C^P cyclometalated complex when they reacted $[MCl_2Cp^*]_2$ (M = Ir, Rh) with 2,4,6-triphenylphosphinine without or with the use of sodium acetate. By comparing the results of the complex formation it was found that the absence of the acetate made sluggish the cyclometalation process as shown in Scheme 1.41.[92]



Scheme 1.41: The formation of C^P cyclometalated half-sandwich complexes

The C^O cyclometalated complexes have rarely been investigated, however. Maitlis *et al.* reported such type of complexes by the metalation of $[Rh(Me_2SO)Me_2Cp^*]$ with benzoic acid (Scheme 1.42).[93]

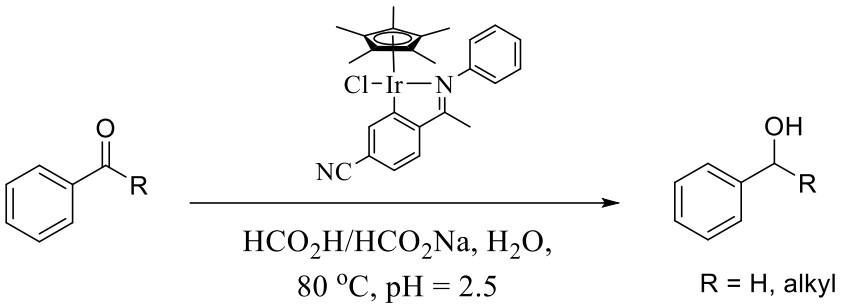


Scheme 1.42: The formation of C^O cyclometalated half-sandwich complexes

On the other hand, the majority of cyclometallated complexes of Ir and Rh reported in literature involve C^N ligands.

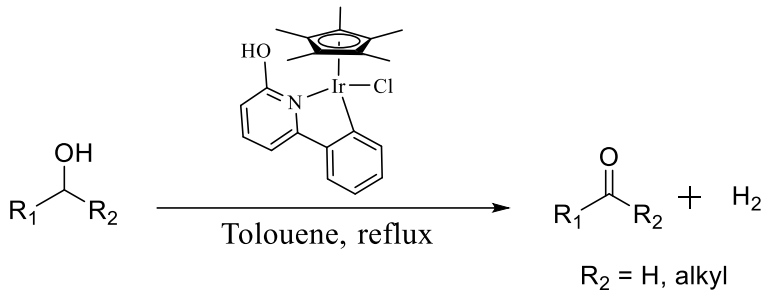
Half-sandwich cyclometalated complexes in particular have been one of the most interesting areas and draw attention from many different fields of chemistry, for example pharmaceutical synthesis and catalysis.[94] Their importance arises from their unique properties such as facile synthesis, robustness, air and moisture stability as well as possible water-solubility. Moreover,

some of the half-sandwich complexes have been shown to have promising biological activity and can be used as anticancer drugs.[95] Of note is that almost all transition metals, such as Pt, Ru, Os, Pd, Rh, and Ir, have been employed for cyclometalation and among all of these, Ir and Rh have received a great deal of attention in catalysis, especially after the reports of Davies and Jones about the reactivity of these complexes towards unsaturated organic molecules.[96,97] Recently, half-sandwich complexes have been used for many catalytic applications, for example, alcohol racemisation, water oxidation, hydrogenation of carbonyl compounds and dehydrogenation of alcohols.[98–102] For example, the iridacycle complex, reported by Wei of our group, exhibited high activity and chemoselectivity for the reduction of aromatic and aliphatic aldehydes in neat water in the presence of sodium formate. The complex was found to be active for the hydrogenation of aldehydes at controlled pH = 2.5 (Scheme 1.43).[36]



Scheme 1.43: Reduction of aldehydes with a half-sandwich cyclometalated complex

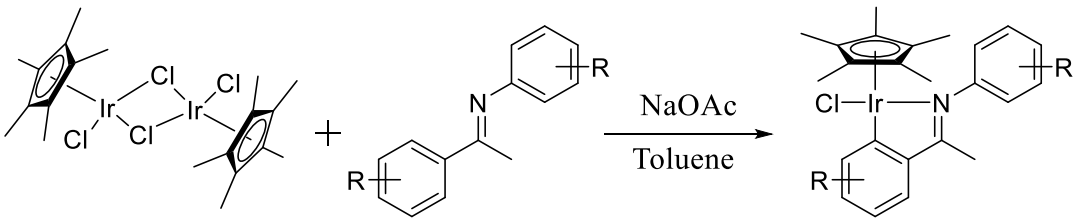
Fujita and co-workers developed a new type of Cp*Ir complexes with a functional C,N-chelate ligand (Scheme 1.44). These complexes were subsequently examined for the oxidation of alcohols. These complexes show high activity for the dehydrogenation of both primary and secondary alcohols.[103]



Scheme 1.44: Oxidation of alcohols with a half-sandwich cyclometalated complex

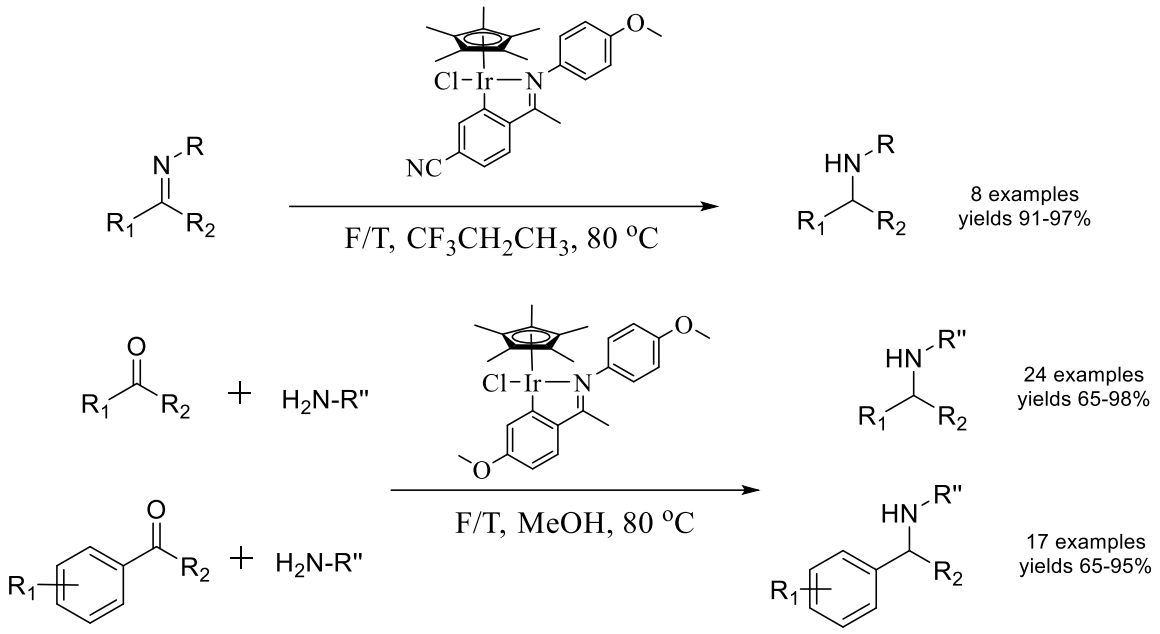
1.8 Previous work within our group

During the last decade, our group reported a family of iridium half-sandwich complexes (iridacycles) by using ketamine ligands (Scheme1.45).[10,104] These versatile complexes allowed efficient activity for the reductive amination of ketones and α-functionalised ketones to give primary and secondary amines. Also, these complexes exhibited excellent results for the TH of aldehydes, ketones and N-heterocyclic compounds in aqueous medium. In addition, these catalysts were found to be not only capable of reducing different multiple functional groups but also capable of dehydrogenating a range of saturated N-heterocyclic compounds. Moreover, these complexes could be used for the oxidant and base free C-C bond formation with functionalised N-heterocycles.[10]



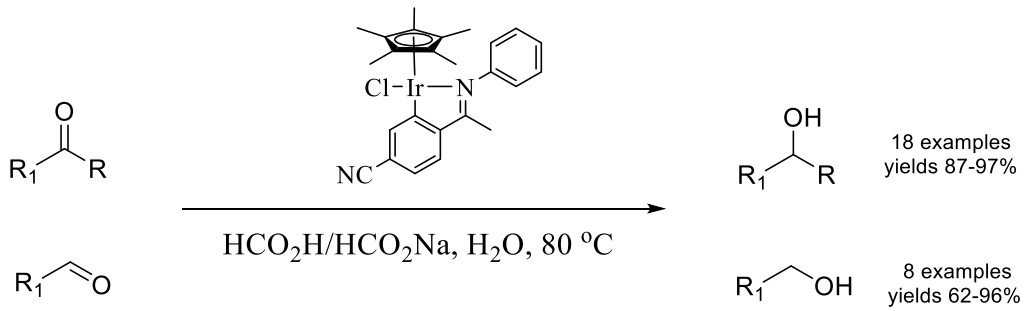
Scheme 1.45: Cyclometalated half-sandwich iridium complexes (iridicycle)

Wang, a group co-worker, reported the imine reduction and reductive amination of various aliphatic and aromatic carbonyl compounds, using the cyclometalated iridium complex in the presence of an azeotropic F/T mixture as a reducing agent as shown in Scheme 1.46.[105]



Scheme 1.46: Cyclometalated Cp*Ir complexes for imine reduction and reductive amination

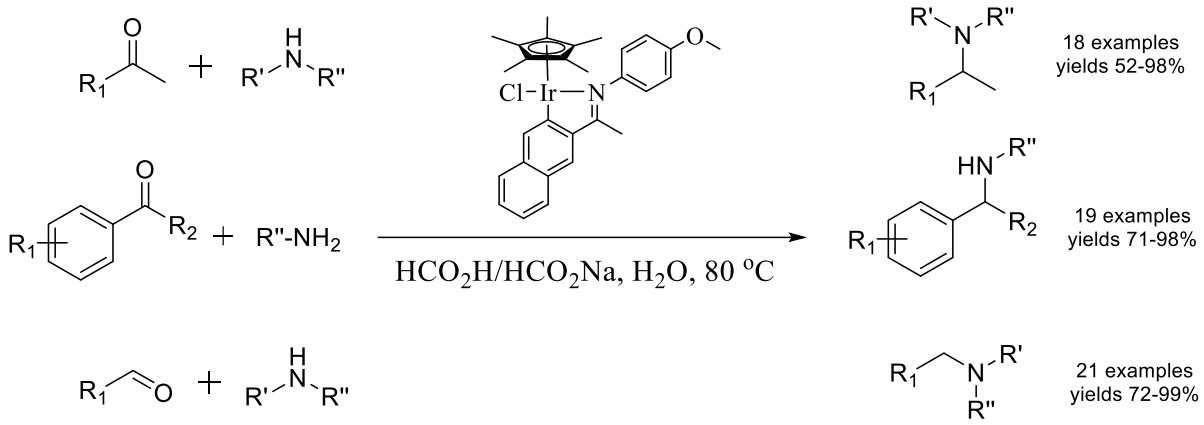
A significant breakthrough for such complexes is the use of water as a reaction solvent under acidic conditions.[106] Reports by Wei *et al.* added another example for the scope of the cyclometalated catalysts. She investigated the reduction of carbonyl compounds in water using sodium formate and formic acid as a hydrogen donor at pH = 2.5. Example are shown in Scheme 1.47.[36]



Scheme 1.47: Cyclometalated Cp*Ir complexes for carbonyl reduction

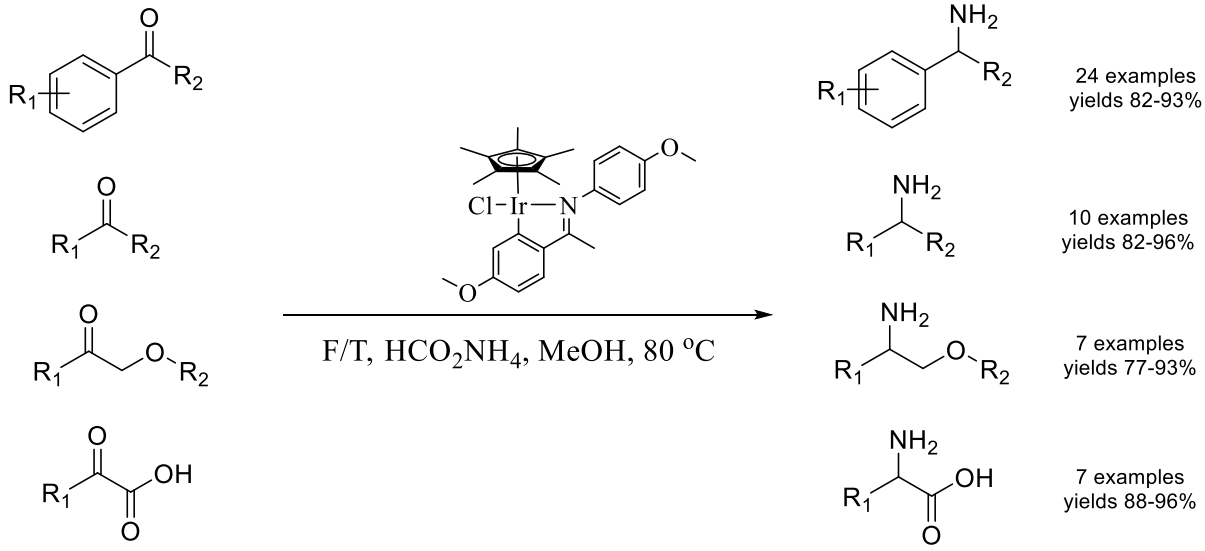
The impressive results of these reactions, together with the ease of ligand synthesis and functionalisation, afforded further investigations towards reductive amination using a range of amines with various aldehydes and ketones in water (Scheme 1.48). The results showed that

the reduction proceeds faster in water than in organic solvents, offering a greener and more efficient method for the reductive amination.[107]



Scheme 1.48: Cyclometalated Cp*Ir complexes for reductive amination in water

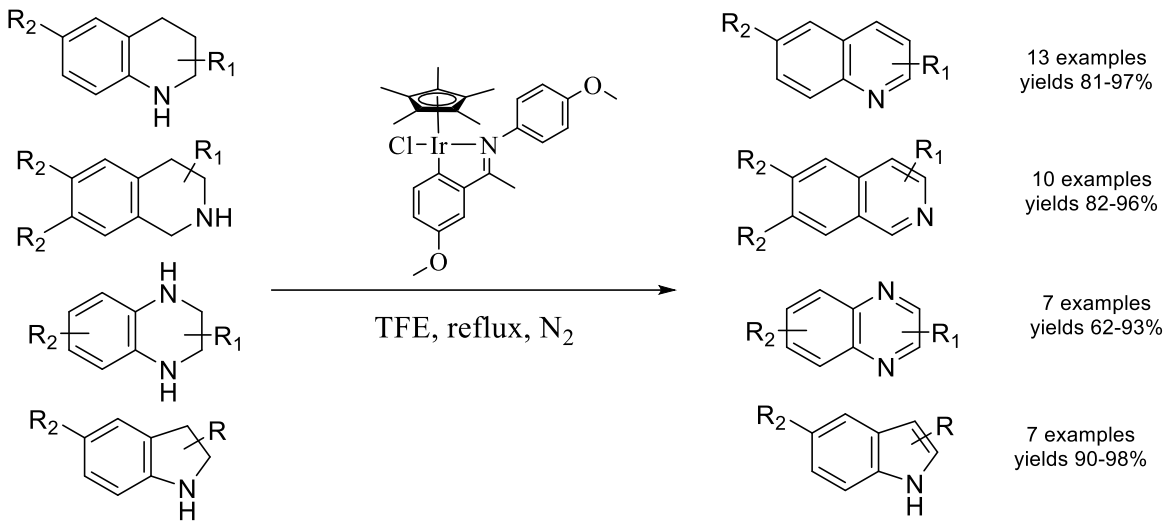
Subsequently, Talwar from the same group reported a productive study of series of cyclometalated iridium complexes, aiming to choose the best iridicycle catalyst for the reductive amination of aromatic and aliphatic ketones, α-keto acids and β-keto ethers by using ammonium formate as a source of hydrogen and amine (Scheme 1.49).[106,108]



Scheme 1.49: Cyclometalated Cp*Ir complexes for reductive amination in ammonium formate

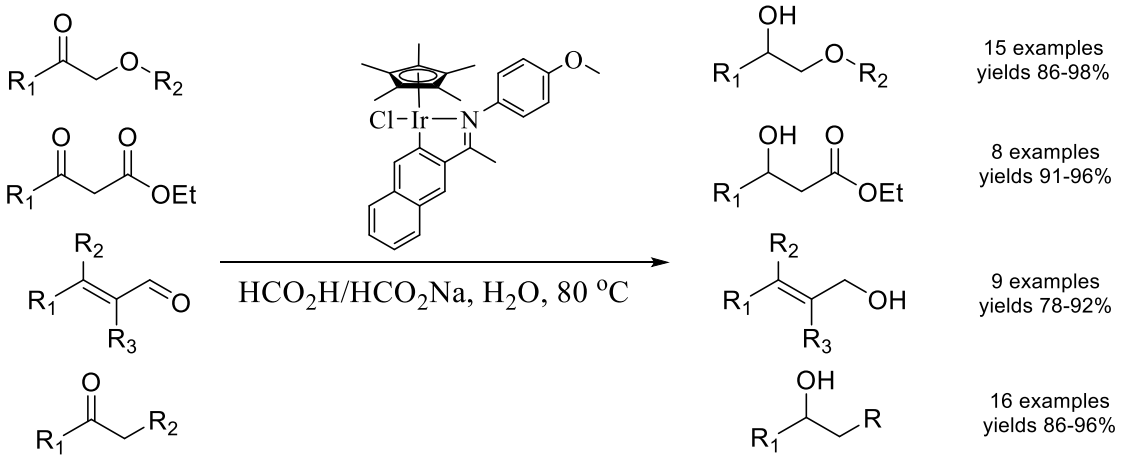
Enormous efforts by the same group were devoted to the development of iridicycle catalysts for more efficient hydrogenation and dehydrogenation of nitrogen heterocycles, including

quinolines, isoquinolines, indoles, quinoxalines, and pyridinium salts under mild conditions (Scheme 1.50).



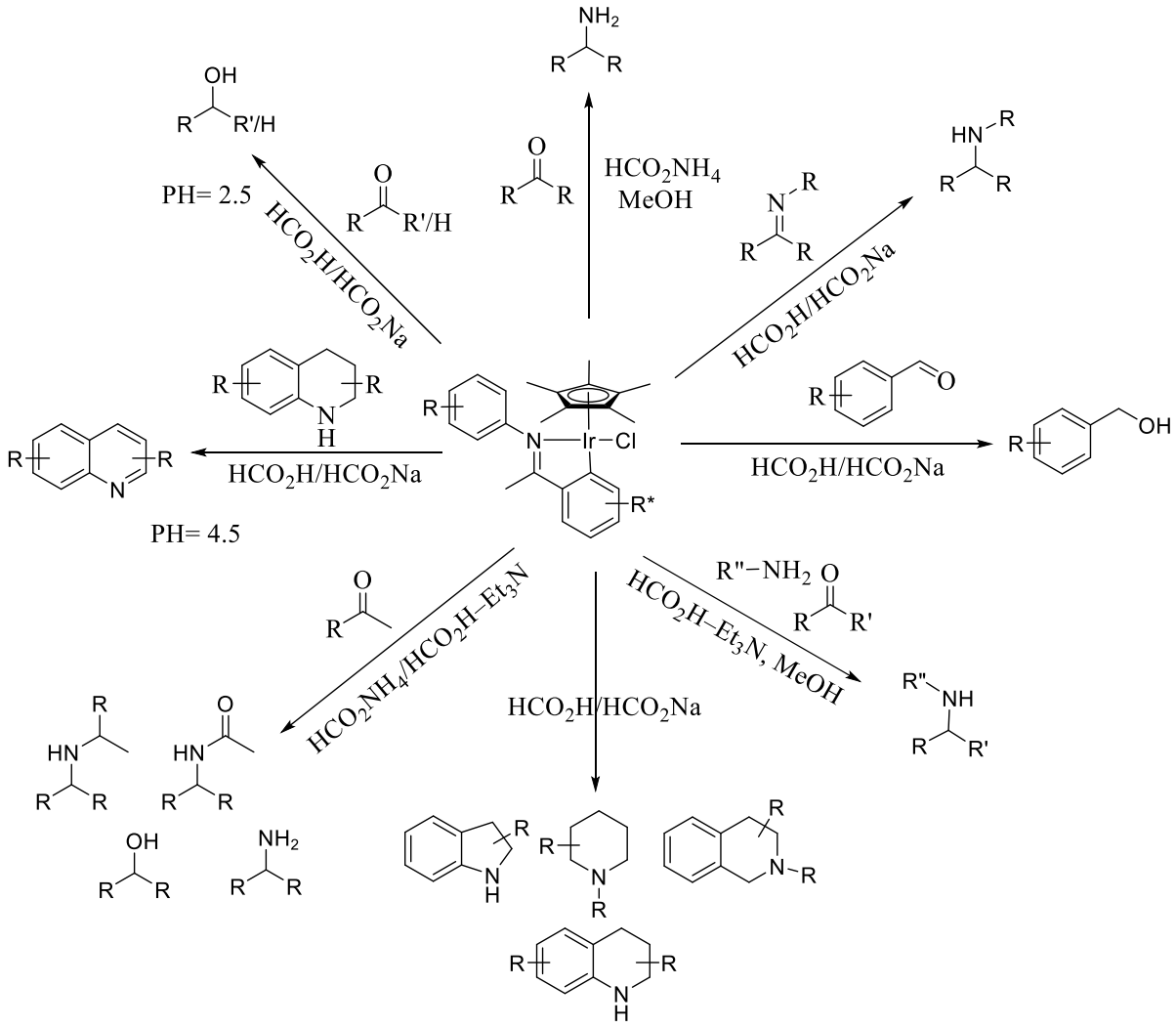
Scheme 1.50: Cyclometalated Cp*Ir complexes for dehydrogenation of nitrogen heterocycles

Also, the group developed a new iridicycle catalyst for the reduction of a wide range of carbonyl groups in water. α-Substituted ketones, β-hydroxy ethers and α,β-unsaturated aldehydes were reduced with excellent results as shown in Scheme 1.51 under these catalytic reactions conditions.[37,109]



Scheme 1.51: Cyclometalated Cp*Ir complexes for carbonyl reduction in water

Selected Examples of the work that reported with the iridicycle complexes in the area of TH are detailed in Scheme 1.52.



Scheme 1.52: Examples of iridacycle complexes reported by our group

Despite the fact that half-sandwich complexes have shown excellent results in hydrogenation and dehydrogenation reactions, the development of a unique system that is capable of TH with a high degree of atom economy, which is still challenging, would be a significant and highly attractive task in this area of research. Also, the use of organic molecules which are viewed as high energy, clean fuels for the future, such as methanol, would be attractive and on demand.

1.9 Aims of the Research

Based on the previous successful results presented by our group involving iridacycle complexes in the area of TH. The aim of the work presented in this thesis is to develop

analogous rhodium complexes, and the main target is to explore the scope of these complexes with the use of methanol as solvent as well as source of hydrogen in TH reactions. In particular, the work will focus on the chemoselective TH of aldehyde compounds and the selective reduction of the C=C double bond of the α,β-unsaturated ketones.

These types of reductions were rarely studied with the use of methanol as a hydrogen donor, and there are only a few reports which described the reduction of the C=C or C=O double bonds using transition metal catalysts under relatively mild conditions. Throughout this thesis we will discuss the use of the developed complexes for the TH of aldehydes to the corresponding alcohol, and the reduction of the C=C double bond preferentially over its C=O counterpart in the α,β-unsaturated carbonyl system under mild conditions. Also, we will present the use of such complexes for the selective reduction of di-aldehydes to produce the hydroxymethyl aldehydes.

1.10 References

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Chapter 2

Transfer hydrogenation of aldehydes via methanol dehydrogenation

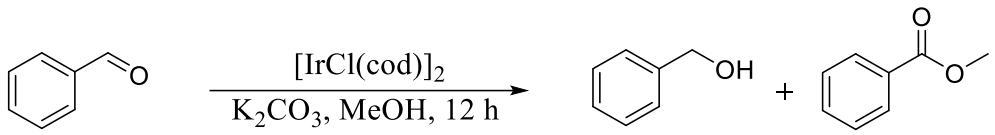
2.1 Introduction

Amongst the numerous transfer hydrogenation reactions reported in the literature, alcohol production from the reduction of corresponding aldehydes or biomass conversions are some of the most common fundamental synthetic transformations in both the chemical and pharmaceutical industries.[1–4] Often, these types of transformations are directly performed using potentially hazardous hydrogen gas or alternatively by using stoichiometric amounts of the reducing agent $NaBH_4$. They can also be carried out by catalytic amounts of organometallic compounds using an alternative hydrogen source, which is called transfer hydrogenation.[3,5,6]

Different metals such as Ir, Ru, Rh, Mn, Au, Pt and Os have been used to accomplish TH reactions,[7–9] and numerous liquids have been used as a source of hydrogen and/or as a solvent. For example, isopropanol,[10] formic acid[11] and formate salts[12] have been employed as convenient hydrogen donors for the TH of carbonyl compounds.

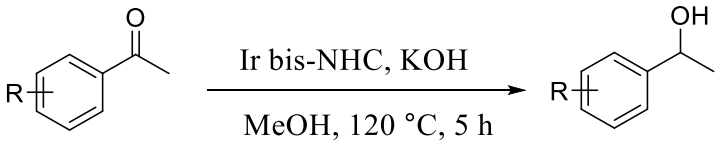
The reduction of an aldehyde with methanol is attractive not only because methanol is an abundant, inexpensive, and easy-to-handle solvent but also because the unique hydrogen carrier ability of methanol (about 12.5 wt% hydrogen);[13,14] however, methanol has been rarely used as a source of hydrogen in particular for TH of aldehydes.[15] Despite the fact that the dehydrogenation of methanol to formaldehyde and dihydrogen is well known to be thermodynamically unfavourable, this reaction is still extremely attractive because the products could serve as intermediates for the production of many useful industrial chemicals.[16–18] Generally, there are limited examples for the use of primary alcohols especially methanol, as a source of hydrogen. This is because their dehydrogenated products (aldehydes) can either poison the catalyst or undergo decarbonylation to produce CO which also deactivates the catalyst.[3] Furthermore, reaction between aldehydes and methanol under basic catalytic

conditions can lead to the corresponding ester by oxidative esterification apart from the hydrogenation product as shown in Scheme 2.1.[19]



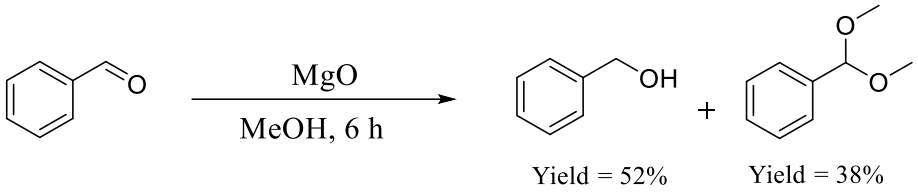
Scheme 2.1: Example of the reduction of aldehydes with methanol

It has been reported that methanol can be used as an inexpensive reagent (solvent and/or hydrogen donor) for the reduction of various functional groups, for example, the reduction of α,β-unsaturated enone,[15,20] alkene and alkyne,[21] and carbonyl compounds.[22] A range of complexes of ruthenium, rhodium, iridium, and osmium show a good activity for such reactions.[15] For example, the iridium catalysts bearing simple ligands were reported by Crabtree *et al.* tolerate air and for efficient TH of ketones with methanol as shown in Scheme 2.2.[17] Benzophenones were successfully reduced to the corresponding alcohols with moderate to good yields, but acetophenones gave poor results, under the applied reaction conditions.



Scheme 2.2: Example of the reduction of ketones in methanol

However, methanol has been less explored in the literature as a hydrogen source for the TH of aldehydes. Pasini *et al.* reported the reduction of furfural with MgO using methanol as a source of hydrogen at 160℃ in 3 hours. Although high yields were obtained under these conditions, a longer reaction time was required for the reduction of benzaldehyde, and a lack of selectivity was observed as shown in Scheme 2.3.[23]



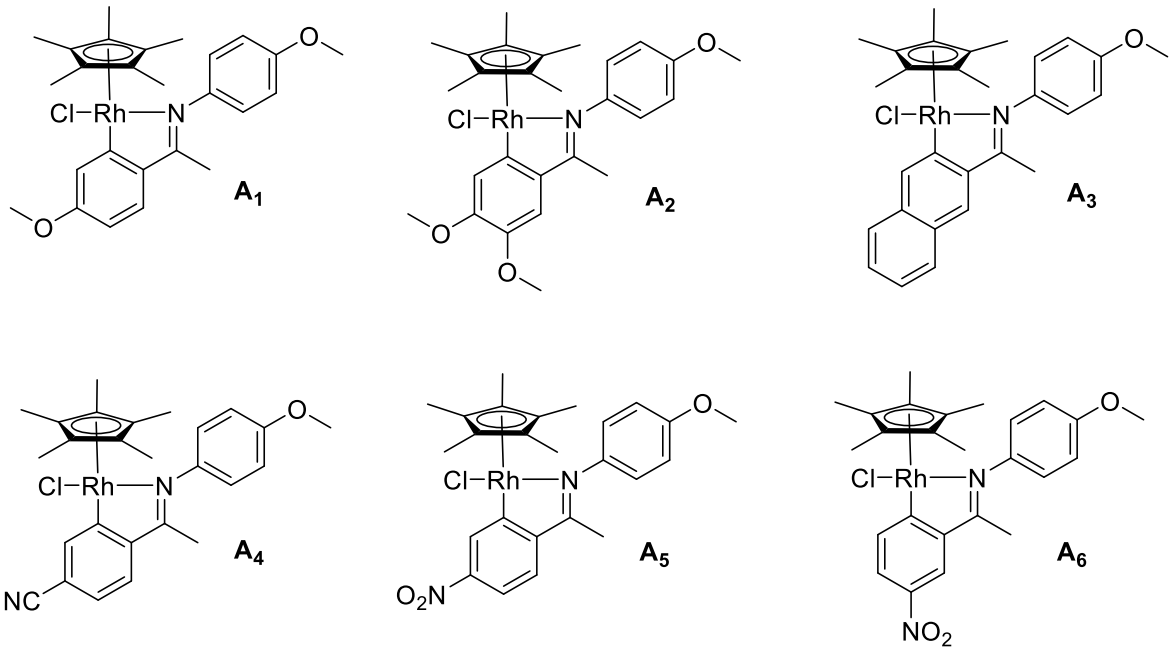
Scheme 2.3: Example of the reduction of aldehydes with methanol

In this chapter, we present our findings concerning the novel cyclometallated rhodium complexes (**A_1** & **A_7**) as shown in Scheme 2.4, for the chemoselective reduction of various aldehydes under mild conditions and with high functional group tolerance. More importantly, methanol has been shown to act not only as the reaction solvent but also as a hydrogen donor.[24]

2.2 Results and discussion

2.2.1 Optimisation of reaction conditions

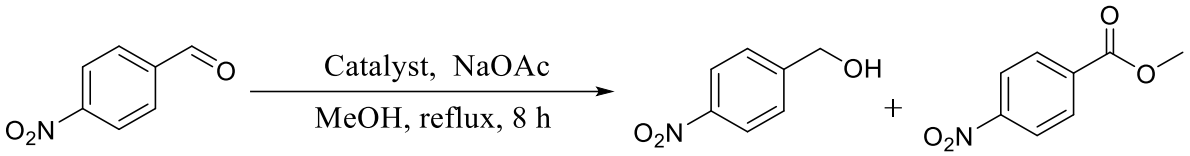
Our work started with the synthesis and development of new rhodium complexes that could be used for TH reactions. The synthesis included preparing a series of rhodium complexes **A_1-A_6** that are shown in Scheme 2.4. This work was based on the use of similar imine ligands to complex with iridium previously reported by our group.[25] These ligands contain either electron-withdrawing groups, such as nitro (-NO_2) and nitrile (-CN) or electron-donating group, such as methoxy (-OCH_3). The development of new complexes involved modifying the imine ligands by replacing -OCH_3 with -OH for the synthesis of **A_7** and **A_8** (Scheme 2.5).



Scheme 2.4: Rhodium complexes screened for TH of aldehydes

Initially, we investigated the reaction between aromatic aldehydes and methanol. Using 4-nitro benzaldehyde as a model substrate, the six complexes were screened in an open vessel under ambient atmosphere for 8 hours, and all reactions were monitored by TLC hourly and analysed by ^{1}H-NMR. The results relating to the type of complex, conversion and the amount of each component (alcohol and ester) are summarised in Table 2.1. The reduction catalysed by $[Cp^*RhCl_2]_2$ in the absence of a ligand resulted in 85% conversion to form 35% alcohol and 44% ester (Table 2.1, Entry 1), while the presence of the ligands showed high selectivity towards the formation of alcohol rather than the ester (Table 2.1, Entries 2-7). Also, the results seem to suggest that the speed of reduction increased by the presence of more electron-rich imine ligands. As observed, electron-withdrawing groups in **A$_4$-A$_6$** showed less conversion efficiency, while the more donating groups have shown higher conversion with full conversion reached with **A$_1$** in 8 hours (Table 2.1, Entry 2).

Table 2.1: Screening of catalyst for the TH of 4-nitro benzaldehyde with methanol

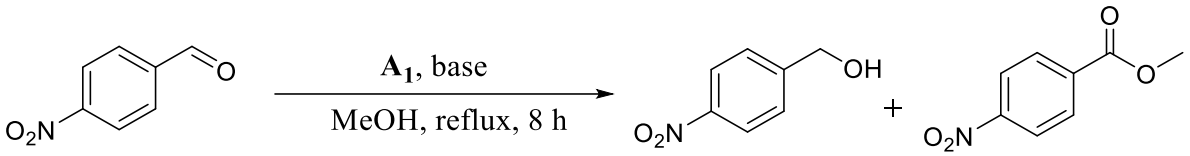


Entry[a]	Catalyst	Conversion %[b]	Alcohol %[c]	Ester %[c]
1	$[Cp^*RhCl_2]_2$	85	35	44
2	**A_1**	100	93	6
3	**A_2**	60	55	2
4	**A_3**	55	47	trace
5	**A_4**	36	34	trace
6	**A_5**	32	28	trace
7	**A_6**	29	25	trace

[a] Reaction conditions: aldehyde (0.25 mmol), catalyst (0.005 mmol), NaOAc (0.5 mmol) and methanol (1.5 mL), stirred at 90 ºC for 8 h. [b] Conversion determined by ^{1}H-NMR spectroscopy. [c] Yield determined by isolated product.

With these observations, **A_1** was adopted for a further subsequent screening of reaction conditions in order to enhance the amount of alcohol product. The results of screening different bases are shown in Table 2.2.

Table 2.2: Screening of base for the TH of 4-nitro benzaldehyde



Entry[a]	**A1** (mol%)	Base	Conversion %	Alcohol %[b]	Ester %[b]
1	2	-	6	trace	0
2	2	NaOAc	100	93	6
3	1	NaOAc	60	57	trace
4	2	Na_2CO_3	100	92	4
5	2	NaOH	100	91	6
6	2	K_2CO_3	100	90	6
7	2	$PhCO_2Na$	98	90	5
8	2	$NaHCO_3$	95	89	3
9	2	$CaCO_3$	<5	0	0
10	2	ZnOAc	0	0	0

[a] Reaction conditions: aldehyde (0.25 mmol), catalyst (0.005 mmol), base (0.5 mmol) and methanol (1.5 mL), stirred at 90 ºC for 8 h. [b] Yield determined by isolated product.

The results of base screening showed that the presence of base was essential for both the catalytic activity and the reaction to proceed to the corresponding alcohol (Table 2.2, Entry 1). However, the use of different bases did not show a significant improvement to shift the reaction towards the ester rather than the alcohol, or increase the selectivity towards alcohol and decrease the formation of ester.

Regarding the catalyst loading, base, and solvent amounts, it was shown that the optimal catalytic efficiency was obtained by the use of 2 mol% catalyst **A_1** and 2 equivalents of sodium acetate (Table 2.2, Entry 2). A lower catalyst loading of 1 mol% or sodium acetate resulted in a clear decrease in conversion (Table 2.2, Entry 3); but the yields were not further improved by increasing the quantity of NaOAc.

We next examined the effect of alcohol solvent (hydrogen donor) using isopropanol and ethanol. Isopropanol gave virtually the same results as those obtained with methanol, while the use of ethanol resulted in a lower reaction conversion of ca 20%. We thought that the catalyst more readily dehydrogenates methanol than ethanol providing more hydride species, and/or that the aldehyde formed from ethanol dehydrogenation (acetaldehyde) could poison the catalyst and reduce the catalyst activity compared to the formaldehyde produced when using methanol.

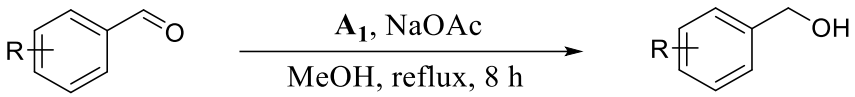
2.2.2 Transfer hydrogenation of aldehydes with methanol

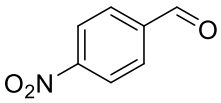
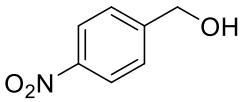
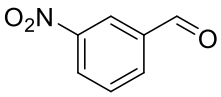
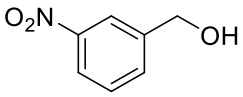
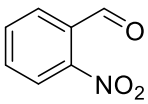
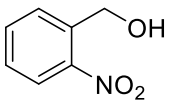
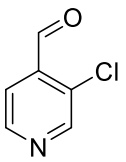
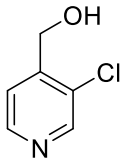
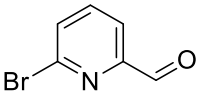
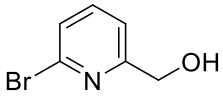
With the optimal reaction condition shown in Table 2.2 (Entry 2), a wide variety of substrates were used for the selective reduction of aldehydes to determine the reaction scope and to evaluate the catalyst performance. The results of the substrate scope in Table 2.3 show that in general **A_1** is efficient to convert aldehydes to benzyl alcohols selectively with good to excellent yields. Different nitro substituents were tolerated, and the desired products were obtained in 83-93% yields (Table 2.3, Entries 1-3). Substituted isonicotinaldehyde and picolinaldehyde were also tolerated and gave the corresponding products in good yields (Table 2.3, Entries 4, 5). Substrates with di-electron-donating or electron-withdrawing groups and those with bulky groups were used and their desired products were achieved in 63-88% (Table 2.3, Entries 20-33). Also, the halo substituents were tolerated, showing hydrodehalogenation

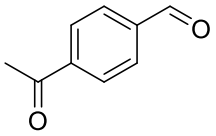
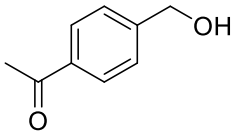
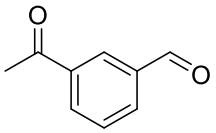
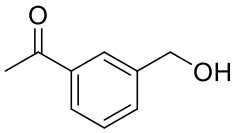
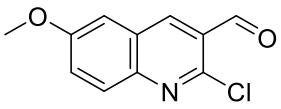
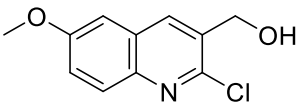
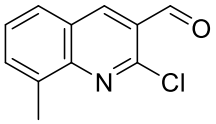
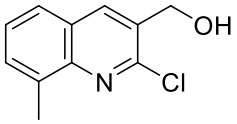
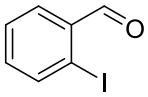
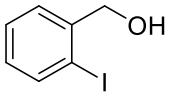
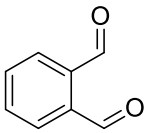
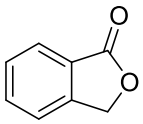
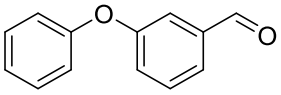
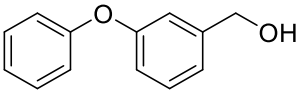
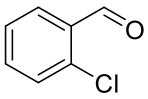
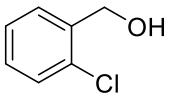
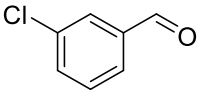
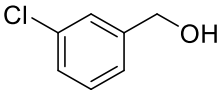
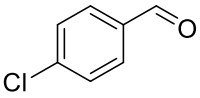
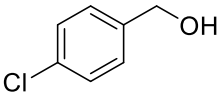
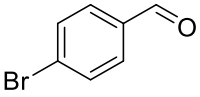
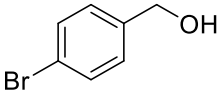
did not take place under the conditions used (Table 2.3, Entries 10, 13, 14, 15, 16, 22-27 and 29).

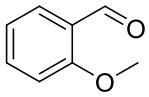
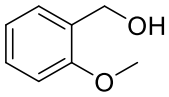
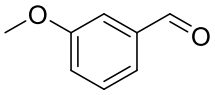
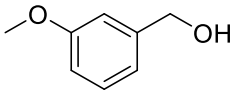
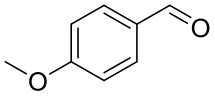
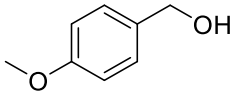
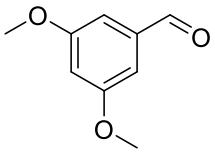
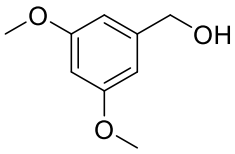
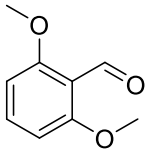
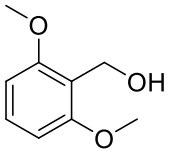
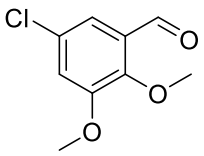
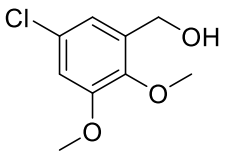
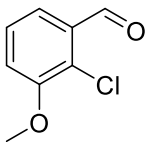
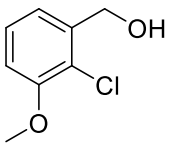
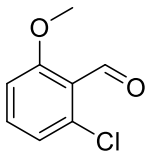
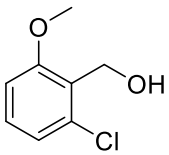
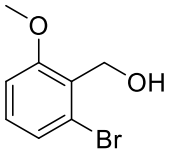
Interestingly, phthalaldehyde (Table 2.3, Entry 11) was successfully reduced selectively to give the afforded product in 75% yield. When the acetyl benzaldehyde was used (Table 2.3, Entry 7), only the aldehyde was reduced, yielding the product in 78% whilst leaving the acyl group intact. This shows that ketones are essentially inactive under the employed conditions.

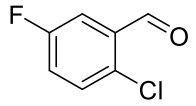
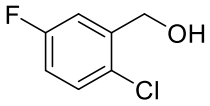
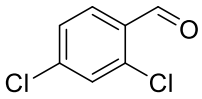
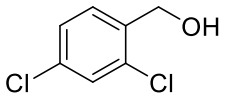
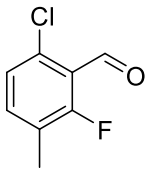
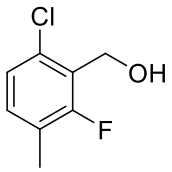
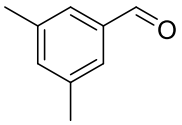
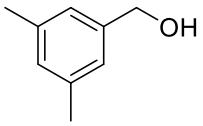
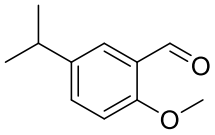
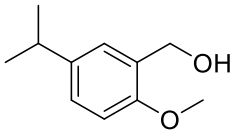
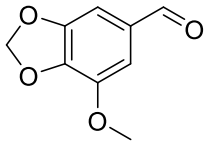
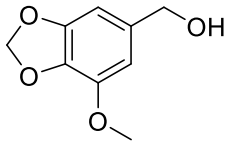
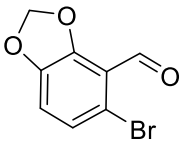
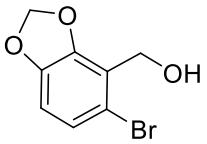
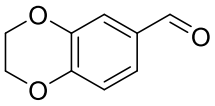
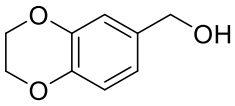
Table 2.3: TH of aldehydes with methanol catalysed by **A_1**



Entry[a]	Substrate	Product	Yield %[b]
1			93
2			83
3			91
4			85
5			89

6			74
7			78
8			80
9			88
10			87
11			75
12			78
13			83
14			85
15			79
16			66

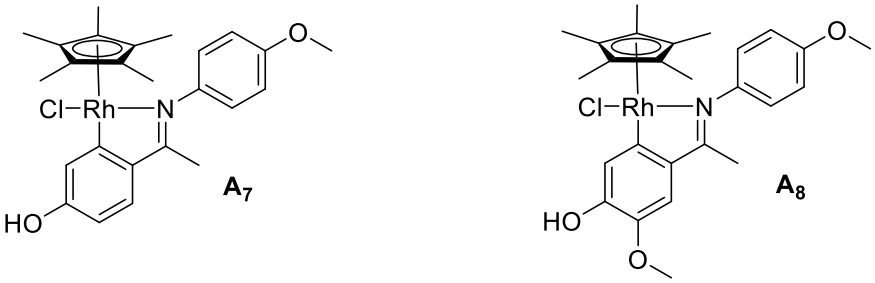
17			82
18			86
19			72
20			82
21			78
22			75
23			87
24			74
25			79

26			78
27			88
28			73
29			63
30			79
31			72
32			73
33			70

[a] Reaction conditions: aldehyde (0.25 mmol), catalyst (0.005 mmol), NaOAc (0.5 mmol) and methanol (1.5 mL), stirred at 90 ºC for 8 h. [b] Yield determined by isolated product.

To confirm the hypothesis that we built up from the information in Table 2.1, that is the speed of reduction is increased by using imine ligands that bear more electron-rich groups, we then synthesised and investigated the activity of related novel complexes **A**$_{7}$ and **A**$_{8}$ against the TH

of aldehydes. The new ligands contain a hydroxyl (-OH) group instead of the methoxy (-OCH_3), which is in *meta* position to the rhodium in complexes **A_7** and **A_8**, as shown in Scheme 2.5. To compare the catalyst-promoted reductions, we tested the model reaction under similar conditions. The results revealed that TH with **A_7** and **A_8** give better conversion than **A_1** in 1 hour reaction time as shown in Table 2.4. The structure of catalyst **A_7** was further determined by X-ray crystallography structure analysis (Figure 1).



Scheme 2.5: Modified rhodium complexes **A_7** and **A_8**

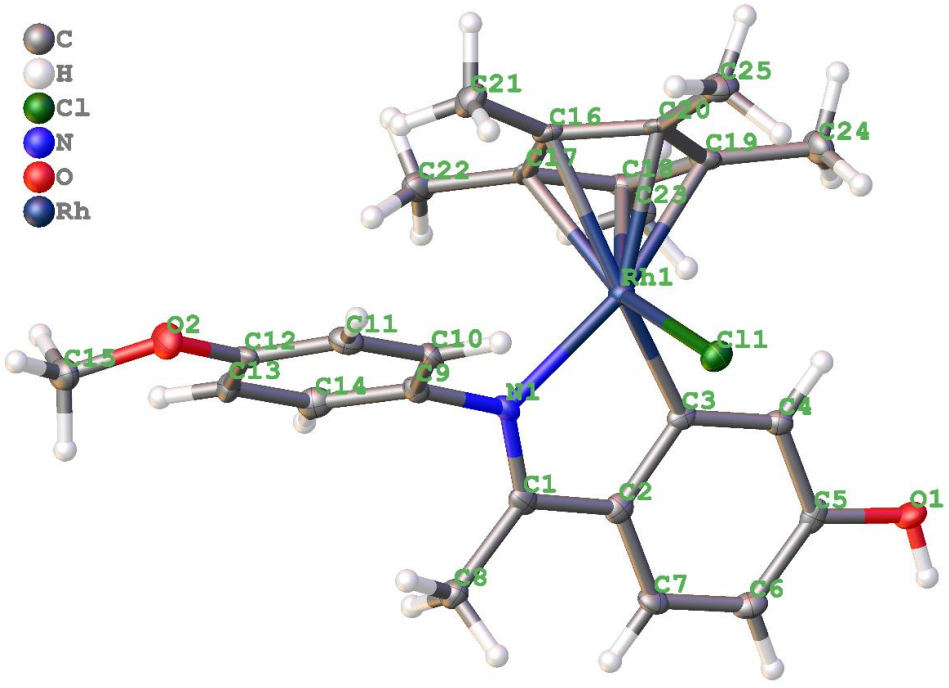
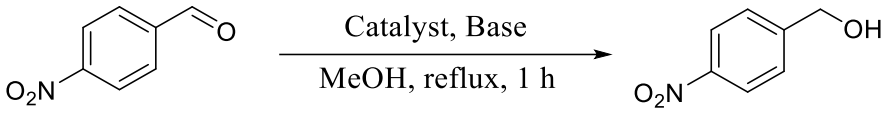


Figure 1: X-ray crystallographic structure of complex **A_7**

Table 2.4: TH of aldehydes with methanol catalysed by **A1**, **A7** and **A8**



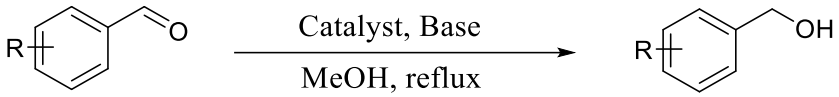
Entry[a]	Catalyst	Cat. (mol%)	Base	Base (equiv.)	Conversion (%)[b]
1	**A1**	2	NaOAc	2	60
2	**A7**	2	NaOAc	2	100
3	**A8**	2	NaOAc	2	88
4	**A1**	1	NaOAc	0.5	40
5	**A7**	1	NaOAc	0.5	91
6	**A8**	1	NaOAc	0.5	70
7	**A1**	1	Cs_2CO_3	0.5	65
8	**A7**	1	Cs_2CO_3	0.5	100
9	**A8**	1	Cs_2CO_3	0.5	84
10	**A7**	0.5	Cs_2CO_3	0.5	70

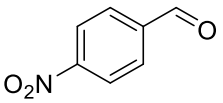
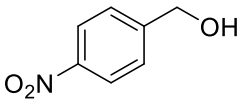
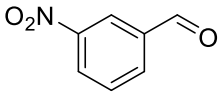
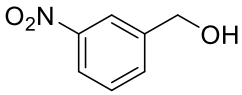
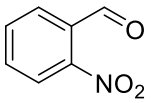
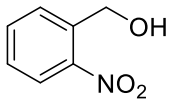
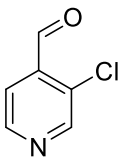
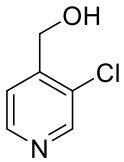
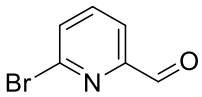
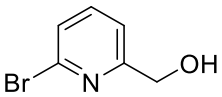
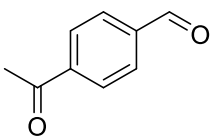
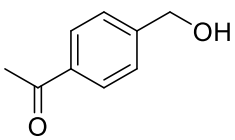
[a] Reaction conditions: aldehyde (0.25 mmol), methanol (1.5 mL), stirred at 90 °C for 1 h. [b] Conversion determined by ^{1}H-NMR spectroscopy.

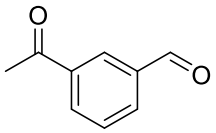
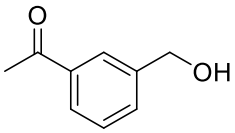
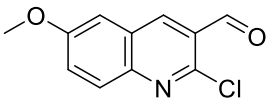
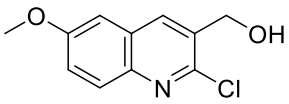
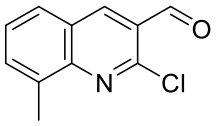
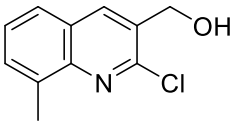
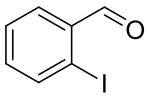
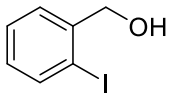
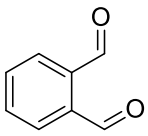
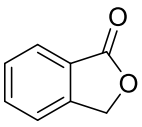
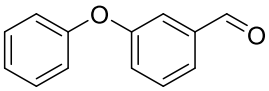
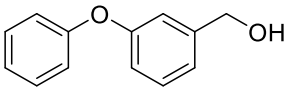
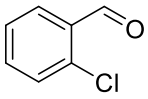
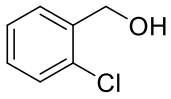
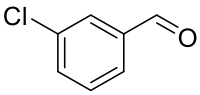
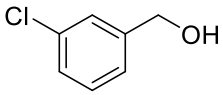
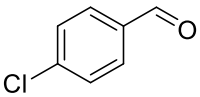
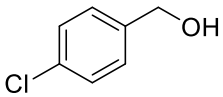
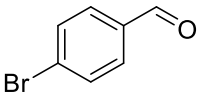
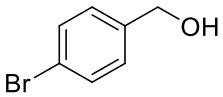
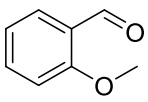
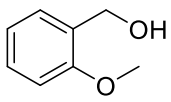
It is evident from Table 2.4 (Entry 1-3) that replacing the -OCH_3 group with a more electron donating -OH group significantly improved the catalyst activity. To show the catalyst performance, we screened the typical reaction by lowering the catalyst loading by half (1.0 mol%). Remarkably, **A7** achieved about 91% conversion in 1 hour (Table 2.4, Entry 5), while **A1** afforded only 40% conversion under the same condition (Table 2.4, Entry 4). Additionally, when we examined the effect of base, Cs_2CO_3 results in full conversion and even when

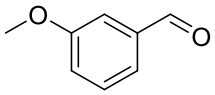
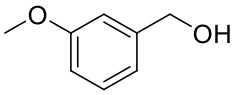
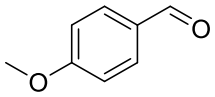
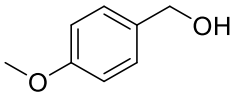
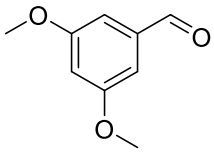
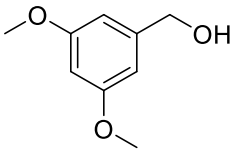
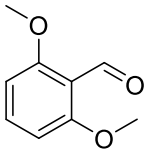
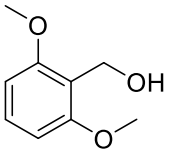
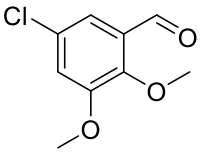
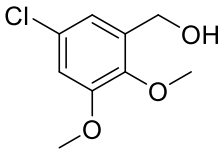
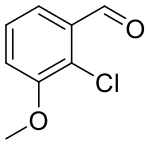
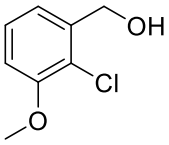
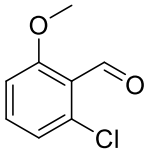
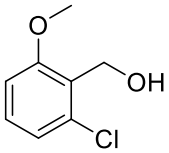
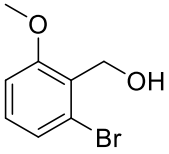
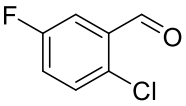
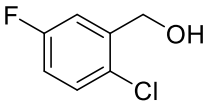
lowering the base loading from 2 to 0.5 equiv. (Table 2.4, Entry 8). However, reducing the amount of catalyst to 0.5 mol% gave only 70% conversion after 6 hours (Table 2.4, Entry 10). Having identified the best reaction condition for complex **A**$_7$, we then repeated our preliminary substrate scope for the TH of aldehydes in methanol and the outcome of the reduction is presented in Table 2.5.

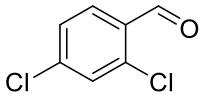
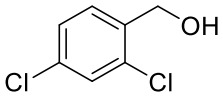
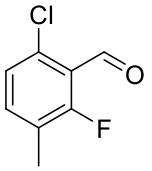
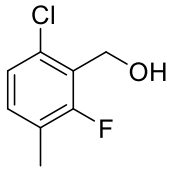
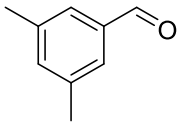
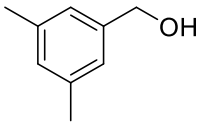
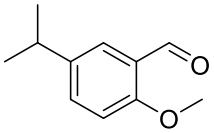
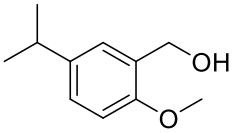
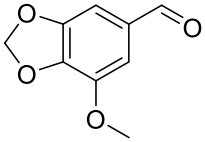
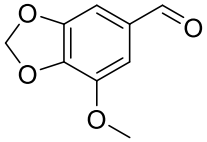
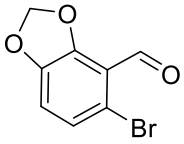
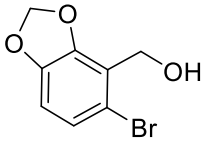
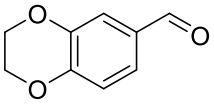
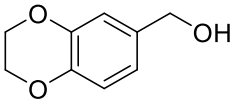
Table 2.5: TH of aldehydes with methanol catalysed by **A**$_7$ and **A**$_1$



Entry	Substrate	Product	**A**$_7$, Yield %[a][b]	**A**$_1$, Yield %[a][c]
1			90	93
2			85	83
3			89	91
4			85	85
5			82	89
6			83	74

7			88	78
8			81	80
9			87	88
10			85	87
11			73	75
12			76	78
13			87	83
14			89	85
15			79	79
16			67	66
17			82	80

18			83	86
19			71	72
20			85	82
21			78	79
22			82	75
23			84	87
24			77	74
25			63	79
26			80	78

27			86	88
28			72	73
29			66	63
30			79	79
31			74	72
32			70	73
33			74	70

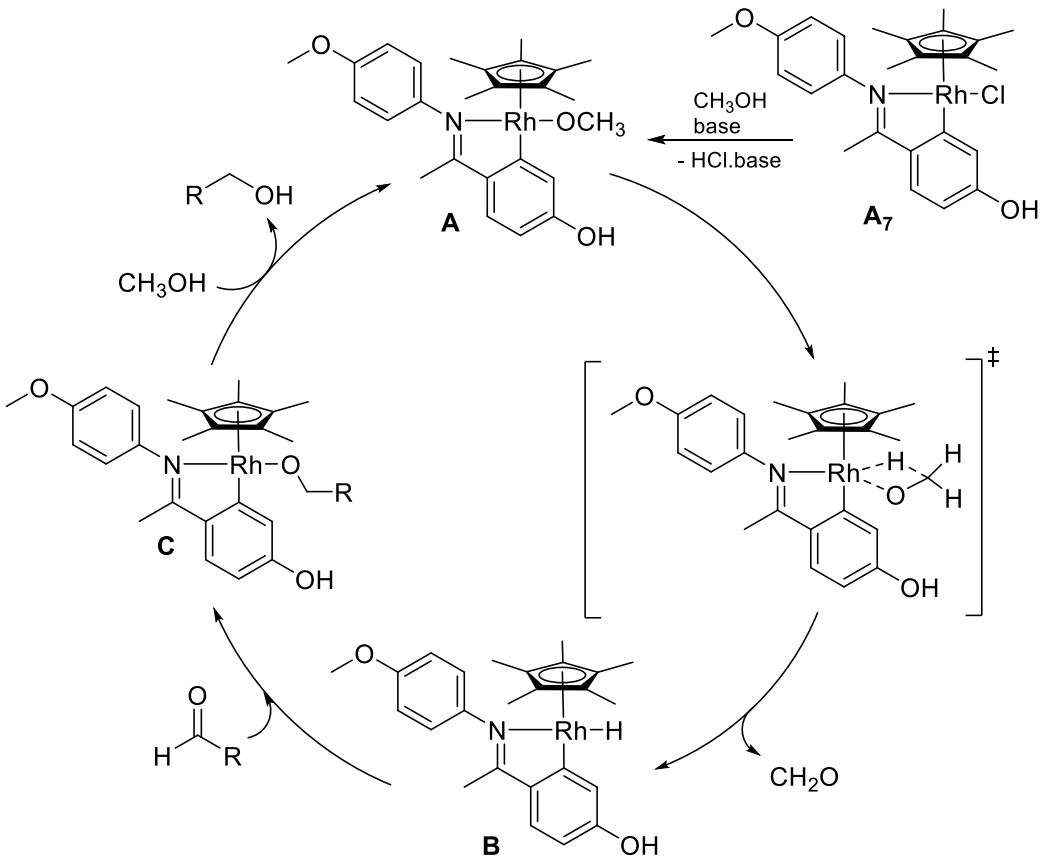
[a] Yield determined by isolated product. [b] Aldehyde (0.25 mmol), catalyst (0.0025 mmol), Cs_2CO_3 (0.125 mmol) and methanol (1.5 mL), stirred at 90 ºC for 1 h. [c] Aldehyde (0.25 mmol), catalyst (0.005 mmol), NaOAc (0.5 mmol) and methanol (1.5 mL), stirred at 90 ºC for 8 h.

As can be seen from Table 2.5, complex **A7** is capable to reduce the aldehyde efficiently in a shorter time and lower catalyst and base loading. By comparing the results of Table 2.5 with the products from Table 2.3, it is shown that aldehydes are reduced leading to their corresponding alcohols with only a slight alteration of the yield. This can explain the advantage effect of the electron-donating group on the catalyst activity. Upon changing from the -OCH_3

to -OH imine ligand, the efficiency of the [Rh-H] intermediate may be improved due to the electron donating ability, of the -OH group which renders the rhodium hydride more hydridic, or the -OH group engaging in hydrogen bonding with the substrate which facilitates the reduction of the substrate.

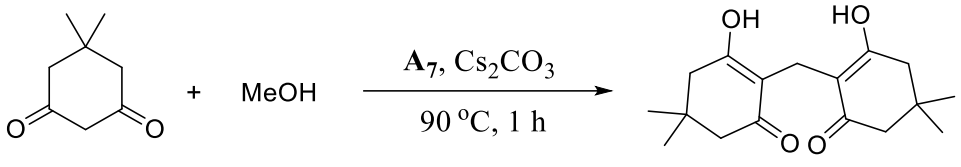
2.2.3 Mechanistic considerations

A proposed catalytic cycle for the TH of aldehydes with methanol is shown in Scheme 2.6. The first step involves the formation of the methoxide complex **A** from the treatment of rhodium complex $\mathbf{A_7}$ with methanol in the presence of a base.[26] This is followed by β-hydrogen elimination of complex **A** via the transition state shown to produce the active Rh-H species **B**. While releasing formaldehyde as a co-product, hydride transfer from the rhodium centre of **B** to the carbonyl of the aldehyde substrate forms the alkoxide **C**. Then methanol protonates complex **C** to give the final alcohol product and regenerates complex **A**. Judging from the distance of chloride to the hydroxyl oxygen (Cl1…O1: 5.71 Å) in complex $\mathbf{A_7}$ (Figure 1), it is unlikely that the hydroxyl group in the ligand could participate in the transition state of hydride formation or transfer via hydrogen bonding, although it may become possible if MeOH is involved.[27]



Scheme 2.6: Proposed catalytic cycle for the TH of aldehydes

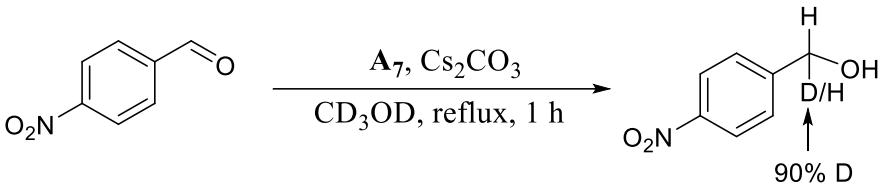
To confirm the suggested mechanistic pathway and also the formation of the reactive and unstable co-product formaldehyde, the model reaction was carried out under the same optimised conditions through replacing the aldehyde substrate with 5,5-dimethyl-1,3-cyclohexanedione (dimedone), which readily undergoes condensation with formaldehyde to give a stable product by elimination of water (Scheme 2.7).[28]



Scheme 2.7: Formation of dimedone-formaldehyde adduct

The presence of this species was confirmed by ^{1}H and ^{13}C NMR in accordance what was reported in the literature and thus verified the formation of formaldehyde during the reaction.[29]

To further elucidate the mechanism and to prove that methanol was the primary and only source of hydrogen during the TH, the reaction was repeated with deuterated methanol (CD_3OD). Confirmed by ^{1}H-NMR, the addition of deuterium across the carbonyl group indicates that methanol acts as both hydrogen donor and solvent as illustrated in Scheme 2.7.



Scheme 2.7: TH of 4-nitrobenzaldehyde with deuterated methanol

Finally, to show the potential application of this catalysed TH, the model reaction was scaled up, using 1g of 4-nitrobenzaldehyde. The substrate was reduced efficiently to give the corresponding alcohol in 87% isolated yield.

2.3 Conclusion

In conclusion, we have developed the first example of a high-yielding selective TH of various aldehydes using methanol as both the reaction solvent and source of hydrogen under moderate conditions, necessitating no inert atmosphere or special equipment. Moreover, the only co-product of this transformation is the gaseous compound formaldehyde which is easily separated from the reaction mixture. The rhodium complex showed high chemoselectivity and efficient transfer hydrogenation towards the reduction of aldehydes in the presence of different functional groups, allowing further transformations to be performed.

2.4 Experimental and analytical data

2.4.1 General information

Unless stated otherwise, all reactions were performed under an open atmosphere using standard techniques. All chemicals that were used in the synthesis of ligands and catalysts were

purchased from commercial suppliers and used as they received i.e. without further purification, and methanol was HPLC grade and used as received. TLC silica gel 60F254 (Merck) plates were used for the analytical thin-layer chromatography and they were revealed under ultra-violet irradiation, potassium permanganate or iodine. All columns were run using a mixture of hexane/ethyl acetate and silica gel 60 Å (230-400 mesh). ^{1}H-NMR and ^{13}C-NMR spectra were recorded with a Bruker 400 MHz spectrometer using $CDCl_3$ as a solvent with tetramethylsilane (TMS) as the internal standard at 25 ºC unless otherwise stated. Processing and interpretation were performed with ACD- labs 12.0 (Advanced Chemistry Development Inc.). The multiplicity of the signals is abbreviated as bs (broad singlet), s (singlet), d (doublet), dd (doublets of doublet), ddd (doublet of doublet of doublet), td (triplets of doublet), or m (multiplet). High-resolution mass spectrum was taken by chemical ionisation (CI) at the Analytical Services of the Department of Chemistry, University of Liverpool. ^{1}H-NMR, ^{13}C-NMR and HRMS for all the products were collected, and the NMR data are consistent with the reported literature.

2.4.2 General procedure for the preparation of imine ligands

Imine ligands were prepared according to the literature.[30] In a 250 mL round-bottomed flask, ketone (5.0 mmol), amine (5.5 mmol) and $NaHCO_3$ (420 mg, 5 mmol) were dissolved in toluene (80 mL). 4Å molecular sieves (1.2 g) were introduced. The resulting mixture was heated under reflux temperature fitted with a dean-stark condenser for 24 h. Afterwards, hot filtration was performed to remove the solid residues, followed by solvent removing under reduced pressure, to afford the crude products which were recrystallized using a hexane/DCM mixture

2.4.3 General procedure for the preparation of rhodium complexes

To a Radleys tube equipped with a stir bar was added $[Cp^*RhCl_2]_2$ dimer (100 mg, 0.16 mmol), imine ligand (2.2 equiv.) and NaOAc (10 equiv.). DCM (10 mL) was then added under a nitrogen atmosphere and the mixture was stirred overnight at room temperature. The resulting mixture was then filtered through Celite® to remove insoluble materials, and dried over $MgSO_4$. Following the filtration, the crude product was dried under vacuum and washed with diethyl ether/hexane to afford an orange air-and moisture-stable pure compound.[30,31]

2.4.4 General procedure for the TH of aldehydes in methanol

Aldehyde (0.25 mmol), catalyst (0.0025 mmol) and Cs_2CO_3 (0.125 mmol) were placed in a Radleys tube followed by the addition of MeOH (1.5 mL). The reaction mixture was then heated to reflux at 90 ºC for 1 h. After completion, the resulting mixture was cooled to room temperature, washed with water, extracted with ethyl acetate, dried over $MgSO_4$ and filtered. The solvent then was removed under vacuum. The resulting crude product was purified by flash chromatography (hexane/ethyl acetate).

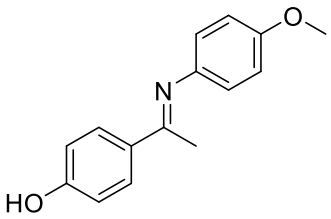
2.4.5 Crystal structure determination of complex A_7

The crystal data collection and structure determination were carried out by Dr. C. Robertson (UoL). Single-crystal X-ray diffraction data for **A_7** were collected on a suitable sample mounted on a Rigaku AFC-12K goniometer using a Rigaku Saturn 724+ are detector and 007HF Molybdenum rotating anode source. Samples were mounted under inert oil using a 10 um MiTeGen tip at 100 K. Data were integrated using SAINT[32] and scaled using SADABS.[33] Structural solution was by direct methods using SHELXT[34] implemented in Olex2[35] and refined on F_o[33] by full-matrix least squares refinement via SHELXL-2013.[36]

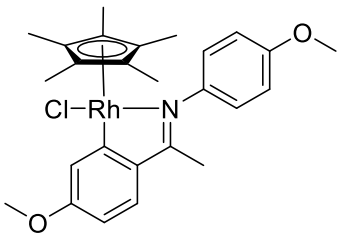
Table 2.7: Crystal data and structure refinement for catalyst **A_7**

Identification code	**A_7**
Empirical formula	$C_{25}H_{29}ClNO_2Rh$
Formula weight	513.85
Temperature/K	100
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	8.6375(3)
b/Å	13.8673(4)
c/Å	18.4717(6)
α/°	90.00
β/°	103.076(3)
γ/°	90.00
Volume/Å^3	2155.15(12)
Z	4
ρ_{calc}g/cm^3	1.584
μ/mm^{-1}	0.939
F(000)	1056.0
Crystal size/mm^3	0.03 × 0.02 × 0.005
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	3.7 to 52.74
Index ranges	$-10 \leq h \leq 10$, $-17 \leq k \leq 17$, $-22 \leq l \leq 23$
Reflections collected	34723
Independent reflections	4406 [R_{int} = 0.1371, R_{sigma} = 0.0711]
Data/restraints/parameters	4406/0/279
Goodness-of-fit on F^2	1.063
Final R indexes [I>=2σ (I)]	R_1 = 0.0477, wR_2 = 0.0794
Final R indexes [all data]	R_1 = 0.0673, wR_2 = 0.0868
Largest diff. peak/hole / e Å^{-3}	0.59/-0.62

2.4.6 Analytical data of imine ligand and rhodium complexes

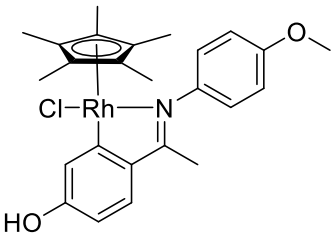


4-Methoxy-N-(1-(4-hydroxyphenyl)ethylidene)aniline: White solid ; m.p. = 120-122 °C, ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.83 (d, J = 8.8 Hz, 2H), 6.90 (d, J = 8.8 Hz, 2H), 6.81 (d, J = 8.8 Hz, 2H), 6.75 (d, J = 8.8 Hz, 2.4 Hz, 2H), 3.81 (s, 3H), 2.22 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 165.90, 158.15, 156.08, 144.68, 132.32, 129.15, 121.19, 115.32, 114.40, 55.64, 17.55; HRMS for $C_{15}H_{15}NO_2$ $[M + H]^+$: m/z calc.: 242.1176; Found: 242.1173.



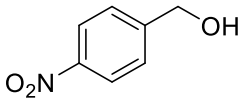
Rhodium complex formed from 4-methoxy-N-(1-(4-methoxyphenyl)ethylidene)aniline:[37] Orange solid; m.p. = 227-229 °C, ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.41 (d, J = 8.5 Hz, 1H), 7.37 (d, J = 2.3 Hz, 1H), 6.93 (d, J = 8.8 Hz, 2H), 6.58 (dd, J = 8.5, 2.3 Hz, 1H), 3.91 (s, 3H), 3.85 (s, 3H), 2.27 (s, 3H), 1.39 (s, 15H). Due to the fluxionality, some of the aromatic hydrogens in **A₁** were invisible at r.t. (see ref 37 for a similar observation); ^{1}H NMR (CD_2Cl_2, 400 MHz, 298 K) δ (ppm): 7.50-7.25 (br m, 4H), 6.96 (d, J = 8.8 Hz, 2H), 6.60 (dd, J = 8.5, 2.3 Hz, 1H), 3.92 (s, 3H), 3.84 (s, 3H), 2.26 (s, 3H), 1.37 (s, 15H); ^{1}H NMR (CD_2Cl_2, 400 MHz, 213 K) δ (ppm): 7.75 (d, J = 8.8 Hz, 1H), 7.41 (d, J = 8.5 Hz, 1H), 7.24 (d, J = 2.0 Hz, 1H), 6.96 (d, J = 8.8 Hz, 1H), 6.86-6.79 (m, 2H), 6.56 (dd, J = 8.5, 2.0 Hz, 1H), 3.85 (s, 3H), 3.79 (s, 3H), 2.22 (s, 3H), 1.28 (s, 15H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 160.98,

157.63, 143.74, 140.82, 129.13, 124.48, 120.82, 108.59, 96.25, 96.19, 55.67, 55.27, 17.17, 8.94. More concentrated sample run in CD_2Cl_2 to resolve quaternary C's and Rh-C coupling; ^{13}C NMR (CD_2Cl_2, 100 MHz, 298 K) δ (ppm): 186.86 (d, J_{Rh-C} = 33 Hz)[9], 178.32, 161.42, 158.18, 144.13, 141.49, 129.31, 124.80, 121.24, 114.30, 108.72, 96.67, 96.61, 56.03, 55.67, 17.31, 9.08; HRMS for $C_{26}H_{31}ClRhNO_2$ $[M - Cl]^+$: m/z calc.: 492.1406; Found: 492.1410.

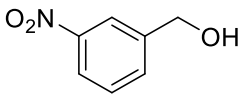


Rhodium complex formed from 4-methoxy-N-(1-(4-hydroxyphenyl)ethylidene)aniline:[37] Orange solid; m.p. = 225-229 °C; ^1H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.26 (d, J = 8.3 Hz, 2H), 7.20 (d, J = 2.3 Hz, 1H), 6.94 (d, J = 8.3 Hz, 2H), 6.43 (dd, J = 8.3, 2.3 Hz, 1H), 3.85 (s, 3H), 2.24 (s, 3H), 1.38 (s, 15H). As with **A₁**, an aromatic hydrogen was invisible at r.t.; ^1H NMR (CD_2Cl_2, 400 MHz, 298 K) δ (ppm): 7.50-7.05 (br m, 4H), 6.96 (d, J = 8.6 Hz, 1H), 6.43 (d, J = 8.2 Hz, 1H), 6.22 (br s, 1H), 3.84 (s, 3H), 2.24 (s, 3H), 1.36 (s, 15H); ^1H NMR (CD_2Cl_2, 400 MHz, 213 K) δ (ppm): 7.73 (d, J = 8.6 Hz, 1H), 7.35 (br s, 1H), 7.14 (d, J = 8.2 Hz, 1H), 7.0 (s, 1H), 6.99 (d, J = 8.6 Hz, 1H), 6.86-6.80 (m, 2H), 6.2 (d, J = 8.2 Hz, 1H), 3.80 (s, 3H), 2.20 (s, 3H), 1.28 (s, 15H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 157.84, 157.62, 143.78, 140.57, 129.33, 122.91, 110.47, 100.15, 96.24, 96.18, 55.69, 17.18, 8.91. More concentrated sample run in CD_2Cl_2 to resolve quaternary C's and Rh-C coupling; ^{13}C NMR (CD_2Cl_2, 100 MHz, 298 K) δ (ppm): 186.53 (d, J_{Rh-C} = 33 Hz)[9], 178.59, 158.40, 158.15, 144.17, 141.03, 129.56, 124.86, 123.38, 114.35, 110.62, 100.58, 96.66, 96.60, 56.05, 17.31, 9.06; HRMS for $C_{25}H_{29}ClRhNO_2$ $[M - Cl]^+$: m/z calc.: 478.1248; Found: 478.1255.

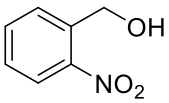
2.4.7 Analytical data of alcohol products



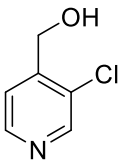
4-Nitrophenylmethanol:[38] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 8.22 (d, J = 8.6 Hz, 2H), 7.54 (d, J = 8.6 Hz, 2H), 4.84 (s, 2H), 1.83 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 148.22, 127.14, 123.90, 64.19; HRMS for $C_7H_7NO_3$ $[M + H]^+$: m/z calc.: 154.0499; found: 154.0503.



3-Nitrophenylmethanol:[39] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 8.23 (s, 1H), 8.14 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.53 (t, J = 8.0 Hz, 1H), 4.82 (s, 2H), 2.21 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 148.53, 143.00, 132.75, 129.58, 122.62, 121.63, 64.10; HRMS for $C_7H_7NO_3$ $[M + H]^+$: m/z calc.: 154.0499; found: 154.0505.

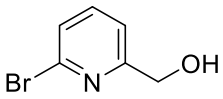


2-Nitrophenylmethanol:[24] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 8.11 (d, J = 8.2 Hz, 1H), 7.75 (d, J = 7.5 Hz, 1H), 7.67 (t, J = 7.5 Hz, 1H), 7.48 (t, J = 7.5 Hz, 1H), 4.98 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 147.83, 136.89, 134.30, 130.18, 128.68, 125.19, 62.75; HRMS for $C_7H_7NO_3$ $[(M - H_2O) + H]^+$: m/z calc.: 136.0393; found: 136.0396.

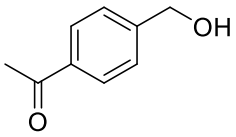


3-Chloropyridin-4-methanol:[40] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 8.51 (s, 1H), 8.50 (d, J = 5.6 Hz, 1H), 7.53 (d, J = 5.2 Hz, 1H), 4.83 (d, J = 5.6 Hz, 2H), 2.3 (t, J = 5.8 Hz,

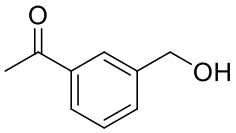
1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 148.88, 148.22, 147.42, 129.76, 121.98, 61.36; HRMS for C_6H_6ClNO $[M + H]^+$: m/z calc.: 144.0211; found: 144.021.



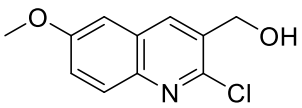
6-Bromopyridin-2-methanol:[41] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.55 (t, J = 7.6, 1H), 7.40 (d, J = 7.6 Hz, 1H), 7.29 (d, J = 7.6 Hz, 1H), 4.75 (s, 2H), 3.15 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 161.33, 141.54, 139.20, 126.81, 119.43, 64.34; HRMS for C_6H_6BrNO $[M + H]^+$: m/z calc.: 187.9706; found: 187.9706.



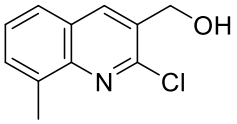
4-Acetyl phenylmethanol:[42] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.93 (d, J = 8.3 Hz, 2H), 7.44 (d, J = 8.3 Hz, 2H), 4.76 (s, 2H), 2.59 (s, 3H), 2.22 (br s, 1H) ; ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 198.14, 146.41, 136.40, 128.74, 126.73, 64.69, 26.78; HRMS for $C_9H_{10}O_2$ $[M + H]^+$: m/z calc.: 151.0754; found: 151.075.



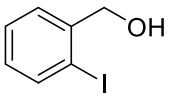
3-Acetyl phenylmethanol:[43] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.94 (s, 1H), 7.86 (d, J = 7.6 Hz, 1H), 7.57 (d, J = 7.6 Hz, 1H), 7.45 (t, J =7.6 Hz, 1H), 4.75 (s, 2H), 2.60 (s, 3H), 2.45 (br s, 1H) ; ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 198.50, 141.60, 137.37, 131.71, 128.90, 127.64, 126.71, 64.77, 26.82; HRMS for $C_9H_{10}O_2$ $[M + H]^+$: m/z calc.: 151.0754; found: 151.0751.



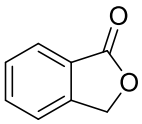
2-Chloro-6-methoxyquinolin-3-methanol:[44] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 8.18 (s, 1H), 7.91 (d, J = 9.2 Hz, 1H), 7.37 (dd, J = 9.2, 2.8 Hz, 1H), 7.09 (d, J = 2.8 Hz, 1H), 4.91 (d, J = 5.6 Hz, 2H), 3.93 (s, 3H), 2.23 (t, J = 5.9 Hz, 1H);^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 158.42, 146.55, 143.05, 135.22, 132.60, 129.76, 128.64, 122.94, 105.34, 62.26, 55.76; HRMS for $C_{11}H_{10}ClNO$ $[M + H]^+$: m/z calc.: 224.0473; found: 224.0475.



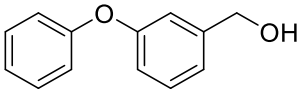
2-Chloro-8-methylquinolin-3-methanol:[45] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 8.24 (s,1H), 7.68 (d, J = 7.9 Hz, 1H), 7.56 (d, J = 7.2 Hz, 1H), 7.45 (t, J = 7.6 Hz, 1H), 4.93 (d, J = 6.0 Hz, 2H), 2.14 (t, J = 6.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 148.20, 146.41, 136.65, 136.61, 132.04, 130.47, 127.56, 127.08, 125.59, 62.34, 17.99; HRMS for $C_{11}H_{10}ClNO_2$ $[M + H]^+$: m/z calc.: 208.04524; found: 208.0524.



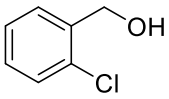
2-Iodophenylmethanol:[46] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.83 (d, J = 7.6 Hz, 1H), 7.46 (d, J = 7.6 Hz, 1H), 7.37 (t, J = 7.6 Hz, 1H), 7.01 (t, J = 7.6 Hz, 1H), 4.69 (d, J = 6.2 Hz, 2H), 1.99 (t, J = 6.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 142.75, 139.37, 129.48, 128.65, 128.64, 97.63, 69.50; HRMS for C_7H_7IO $[(M – H_2O) + H]^+$: m/z calc.: 216.9509; found: 216.9514.



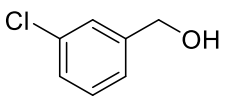
Isobenzofuran-1(3H)-one:[47] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.92 (d, J = 7.6 Hz, 1H), 7.69 (t, J = 7.6 Hz, 1H), 7.54 (t, J = 7.6 Hz, 1H), 7.50 (d, J = 7.6 Hz, 1H), 5.34 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 171.25, 146.63, 134.14, 129.16, 125.90, 125.83, 122.22, 69.79; HRMS for $C_8H_6O_2$ $[M + H]^+$: m/z calc.: 135.0441; found: 135.0444.



3-Phenoxyphenylmethanol:[48] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.36-7.26 (m, 3H), 7.13-7.04 (m, 2H), 7.00 (d, J = 7.5 Hz, 3H), 6.91 (d, J = 8.2 Hz, 1H), 4.62 (s, 2H), 2.04 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 157.72, 157.14, 143.06, 130.01, 129.91, 123.51, 121.65, 119.17, 118.04, 117.21, 65.07; HRMS for $C_{13}H_{12}O_2$ $[M + H]^+$: m/z calc.: 201.091; found: 201.0914.

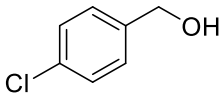


2-Chlorophenylmethanol:[24] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.49 (d, J = 7.2 Hz, 1H), 7.37 (d, J = 7.6 Hz, 1H), 7.28 (t, J = 7.2, Hz, 1H), 7.24 (t, J = 7.6 Hz, 1H), 4.79 (d, J = 6.3 Hz, 2H), 1.93 (t, J = 6.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 138.26, 132.84, 129.47, 128.97, 128.86, 127.15, 62.99; HRMS for C_7H_7ClO $[(M - H_2O) + H]^+$: m/z calc.: 125.0153; found: 125.0155.

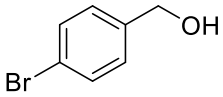


3-Chlorophenylmethanol:[49] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.36 (s, 1H), 7.32-7.20 (m, 3H), 4.67(s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 142.93, 134.55,

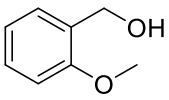
129.94, 127.83, 127.07, 124.96, 64.63; HRMS for C_7H_7ClO [(M – H_2O) + H]$^+$: m/z calc.: 125.0153; found: 125.0154.



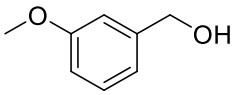
4-Chlorophenylmethanol:[38] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.36-7.28 (m, 4H), 4.67 (d, J = 5.2 Hz, 2H), 1.73 (br t, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 139.37, 133.50, 128.82, 128.41, 64.72; HRMS for C_7H_7ClO [(M – H_2O) + H]$^+$: m/z calc.: 125.0153; found: 125.0155.



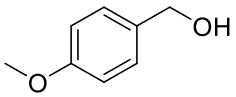
4-Bromophenylmethanol:[38] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.48 (d, J = 8.3 Hz, 1H), 7.23 (d, J = 8.3 Hz, 2H), 4.64 (s, 2H), 1.82 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 139.89, 131.76, 128.72, 121.59, 64.72; HRMS for C_7H_7BrO [(M – H_2O) + H]$^+$: m/z calc.: 168.9647; found: 168.9646.



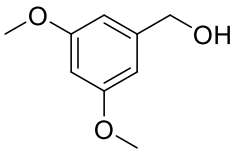
2-Methoxyphenylmethanol:[50] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.32-7.24 (m, 2H), 6.95 (t, J = 7.4 Hz, 1H), 6.89 (d, J = 8.2 Hz, 1H), 4.68 (s, 2H), 3.87 (s, 3H), 2.38 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 157.57, 129.12, 129.10, 128.89, 120.77, 110.31, 62.30, 55.38; HRMS for $C_8H_{10}O_2$ [(M – H_2O) + H]$^+$: m/z calc.: 121.0648; found: 121.0651.



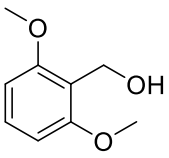
3-Methoxyphenylmethanol:[42] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.31-7.25 (m, 1H), 6.97-6.92 (m, 2H), 6.86-6.81 (m, 1H), 4.68 (s, 2H), 3.82 (s, 3H), 1.72 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 159.96, 142.64, 129.75, 119.23, 113.42, 112.36, 65.43, 55.37; HRMS for $C_8H_{10}O_2$ $[M + H]^+$: m/z calc.: 139.0754; found: 139.0756.



4-Methoxyphenylmethanol:[51] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.29 (d, J = 8.6 Hz, 2H), 6.89 (d, J = 8.6 Hz, 2H), 4.61 (s, 2H) 3.81 (s, 3H), 1.64 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 159.35, 133.25, 128.78, 114.10, 65.20, 55.44; HRMS for $C_8H_{10}O_2$ $[(M - H_2O) + H]^+$: m/z calc.: 121.0648; found: 121.0652.

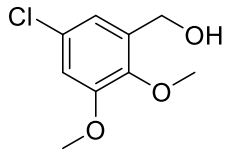


3,5-Dimethoxyphenylmethanol:[52] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 6.48 (d, J = 2.10 Hz, 2H), 6.35 (d, J = 2.10 Hz, 1H), 4.56 (s, 2H), 3.75 (s, 6H), 2.65 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 161.10, 143.50, 104.67, 99.76, 65.46, 55.48; HRMS for $C_9H_{12}O_3$ $[M + H]^+$: m/z calc.: 169.0859; found: 169.0863.

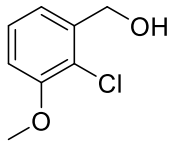


2,6-Dimethoxyphenylmethanol:[53] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.22 (t, J = 8.4 Hz, 1H), 6.56 (d, J = 8.4 Hz, 2H), 4.79 (d, J = 6.3 Hz, 2H), 3.84 (s, 6H), 2.49 (t, J = 6.3 Hz,

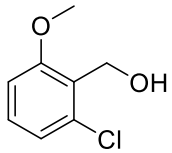
1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 158.53, 129.25, 117.16, 103.94, 55.86, 54.85; HRMS for $C_9H_{12}O_3$ $[(M - H_2O) + H]^+$: m/z calc.: 151.0754; found: 151.0754.



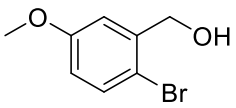
5-Chloro-2,3-dimethoxyphenylmethanol: ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 6.95 (s, 1H), 6.85 (s, 1H), 4.66 (s, 2H), 3.85 (br s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 153.08, 145.52, 135.74, 129.18, 120.29, 112.62, 61.09, 61.01, 56.15; HRMS for $C_9H_{11}ClO_3$ $[(M - H_2O) + H]^+$: m/z calc.: 185.0364; found: 185.0364.



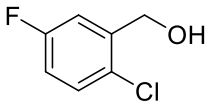
2-Chloro-3-methoxyphenylmethanol:[54] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.25 (t, J = 8.0 Hz, 1H), 7.10 (d, J = 8.0 Hz, 1H), 6.90 (d, J = 8.0 Hz, 1H), 4.79 (d, J = 6.2 Hz, 2H), 3.91(s, 3H), 2.02 (t, J = 6.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 155.18, 139.91, 127.52, 120.96, 120.54, 111.31, 63.19, 56.42; HRMS for $C_8H_9ClO_2$ $[(M - H_2O) + H]^+$: m/z calc.: 155.0258; found: 155.0263.



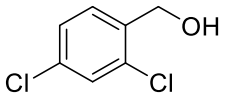
2-Chloro-6-methoxyphenylmethanol: ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.23 (d, J = 7.6 Hz, 1H), 7.13 (t, J = 7.6 Hz, 1H), 7.09 (d, J = 7.6 Hz, 1H), 4.83 (s, 2H), 2.46 (s, 3H), 1.93 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 139.75, 136.05, 134.97, 129.35, 129.17, 127.44, 59.77, 19.82; HRMS for $C_8H_9ClO_2$ $[(M - Cl) + H]^+$: m/z calc.: 139.0309; found: 139.0309.



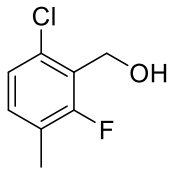
2-Bromo-5-methoxyphenylmethanol:[55] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.40 (d, J = 8.7 Hz, 1H), 7.05 (d, J = 3.1 Hz, 1H), 6.71 (dd, J = 8.7, 3.1 Hz, 1H), 4.69 (s, 2H), 3.79 (s, 3H), 2.25 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 159.37, 140.85, 133.26, 114.89, 114.35, 112.62, 65.13, 55.64; HRMS for $C_8H_9BrO_2$ $[(M - H_2O) + H]^+$: m/z calc.: 198.9753; found; 198.976.



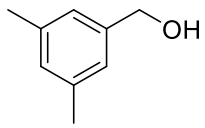
2-Chloro-5-fluorophenylmethanol: ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.30 (dd, J = 8.7, 5.0 Hz, 1H), 7.26 (dd, J = 8.7, 3.1 Hz, 1H), 6.94 (td, J = 8.7, 3.1 Hz, 1H), 4.76 (d, J = 4.2 Hz, 2H), 2.08 (br t, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 161.77 (d, J_{C-F} = 246.4 Hz), 140.54 (d, J_{C-F} = 7.3 Hz), 130.57 (d, J_{C-F} = 8.2 Hz), 126.98 (d, J_{C-F} = 3.2 Hz), 115.58 (d, J_{C-F} = 18.6 Hz), 115.34 (d, J_{C-F} = 19.6 Hz), 62.42 (d, J_{C-F} = 1.2 Hz); HRMS for C_7H_6ClFO $[(M - H_2O) + H]^+$: m/z calc.: 143.0058; found: 143.0063.



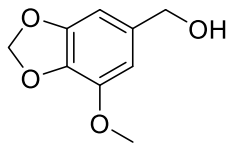
2,4-Dichlorophenylmethanol:[56] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.44 (d, J = 8.2 Hz, 1H), 7.38 (s, 1H), 7.27 (d, J = 8.2 Hz, 1H), 4.75 (s, 2H), 1.99 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 136.89, 133.97, 133.32, 129.56, 129.27, 127.42, 62.35; HRMS for $C_7H_6Cl_2O$ $[(M - H_2O) + H]^+$: m/z calc.: 158.9763; found: 158.977.



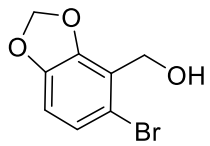
6-Chloro-2-fluoro-3-methylphenyl-methanol: ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.11-7.04 (m, 2H), 4.83 (d, J = 4.0 Hz, 2H), 2.25 (d, J = 2.2 Hz, 3H), 2.13 (br t, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 160.03 (d, J_{C-F} = 248.5 Hz), 132.44 (d, J_{C-F} = 5.3 Hz), 131.49 (d, J_{C-F} = 6.5 Hz), 125.56 (d, J_{C-F} = 18.9 Hz), 124.83 (d, J_{C-F} = 4.0 Hz), 124.16 (d, J_{C-F} = 18.9 Hz), 56.52 (d, J_{C-F} = 5.3 Hz), 14.51 (d, J_{C-F} = 4.0 Hz); HRMS for C_8H_6ClFO [(M – H_2O) + H]$^+$: m/z calc.: 157.0215; found: 157.0218.



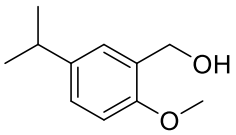
3,5-Dimethylphenylmethanol:[57] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 6.97 (s, 2H), 6.93 (s, 1H), 4.61 (s, 2H), 2.32 (s, 6H), 1.70 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 140.94, 138.31, 129.39, 124.97, 65.56, 21.38; HRMS for $C_9H_{12}O$ [(M – H_2O) + H]$^+$: m/z calc.: 119.0855; found: 119.0855.



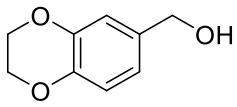
7-Methoxybenzo[d][1,3]dioxol-5-methanol:[58] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 6.54 (s, 1H), 6.53 (s, 1H), 5.95 (s, 2H), 4.56 (s, 2H), 3.89 (s, 3H), 1.90 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 149.03, 143.76, 135.69, 134.72, 106.56, 101.57, 101.43, 65.46, 56.66; HRMS for $C_9H_{10}O_4$ [(M – H_2O) + H]$^+$: m/z calc.: 165.0546; found: 165.0547.



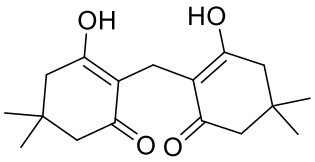
5-Bromobenzo[d][1,3]dioxol-4-methanol:[59] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.02 (d, J = 8.3 Hz, 1H), 6.64 (d, J = 8.3 Hz, 1H), 6.00 (s, 2H), 4.74 (s, 2H), 2.26 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 147.29, 147.25, 125.40, 121.78, 115.14, 109.30, 102.00, 59.64; HRMS for $C_8H_7BrO_3$ $[(M - H_2O) + H]^+$: m/z calc.: 212.9546; found: 202.9547.



5-Isopropyl-2-methoxyphenylmethanol:[60] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.12 (m, 2H), 6.81 (d, J = 8.0 Hz, 1H), 4.67 (d, J = 5.0 Hz, 2H), 3.84 (s, 3H), 2.86 (septet, J = 6.9 Hz, 1H), 2.38 (t, J = 5.0 Hz, 1H), 1.22 (d, J = 6.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 155.72, 141.25, 128.86, 127.14, 126.59, 110.25, 62.60, 55.49, 33.46, 24.34; HRMS for $C_{11}H_{16}O_2$ $[(M - H_2O) + H]^+$: m/z calc.: 163.1117; found: 163.1123.



2,3-Dihydrobenzo[b][1,4]dioxin-6-methanol:[61] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 6.89-6.78 (m, 3H), 4.53 (s, 2H), 4.23 (s, 4H), 2.02 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 143.60, 143.19, 134.46, 120.39, 117.41, 116.32, 65.05, 64.47; HRMS for $C_9H_{10}O_3$ $[(M - H_2O) + H]^+$: m/z calc.: 149.0597; found: 149.0598.



2,2'-Methylenebis(3-hydroxy-5,5-dimethylcyclohex-2-en-1-one):[29] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 11.57 (br s, 2H), 3.16 (s, 2H), 2.29 (s, 4H), 2.28 (s, 4H), 1.05 (s, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 189.68, 113.63, 46.15, 31.94, 29.66, 27.24, 16.10.

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Chapter 3

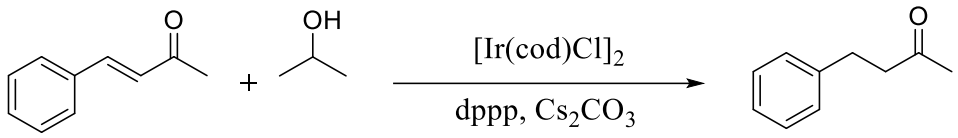
Chemoselective reduction of α,β-unsaturated ketones via methanol dehydrogenation

3.1 Introduction

The TH of α,β-unsaturated carbonyl compounds has great importance from both academic and industrial point of view. This is due to the potential applications of the resulting products in the synthesis of food sweeteners, flavours, perfume, pharmaceuticals and advanced functional materials.[1–4] Actually, the reduction of α,β-unsaturated ketones can follow three different pathways. First, the chemoselective reduction of carbonyl group (1,2-reduction) into allylic alcohol, the second involves the chemoselective reduction of the conjugated alkene (1,4-addition) to give the saturated ketone, and the third is the non-selective reduction of both groups to form the corresponding saturated alcohol.[4–7] As a result of these pathways, a mixture of products are frequently obtained; therefore, numerous methodologies of highly efficient catalytic systems have been developed to promote the selective reduction of the conjugated ketones. It is worth mentioning that the catalytic chemoselective hydrogenation of α,β-unsaturated ketones using an alcohol as either a hydrogen source or reaction solvent has been applied to a wide range of conjugated ketones.[8] Noyori *et al.* presented ruthenium di-amine-diphosphine complex as an excellent precatalyst for the selective reduction of the carbonyl group in a wide range of α,β-unsaturated ketones.[2]

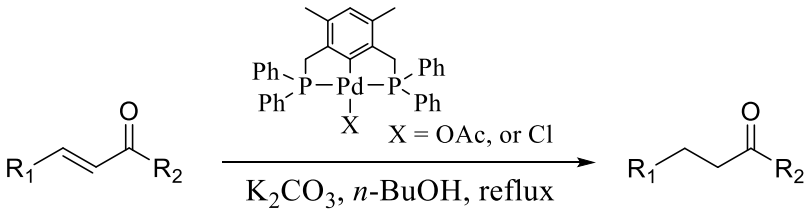
On the other hand, the TH of the olefinic bond of α,β-unsaturated ketones to the saturated ketones is also important for the manufacturers of fragrances and other fine chemicals.[9] However, it remains limited due to the relative ease of reduction of carbonyl group under the stated reaction conditions.[8,10,11] Sasson *et al.* reported earlier the selective reduction of α,β-unsaturated ketones into saturated ketones with a ruthenium catalyst using primary or secondary alcohol as a hydrogen donor. Depending on the type of hydride source, the required temperature for this TH varied between 100-200 ºC.[12] Later on, a variety of metal complexes such as Pd, Rh, Pt, Ni, Ir and Co were used in the presence of different alcohols to perform the

selective hydrogenation of C=C double bond of α,β-unsaturated ketones.[13,14] For example, Sakaguchi *et al.* presented the use of 2-propanol as a hydrogen donor for the selective reduction of the olefinic bond with [Ir(cod)Cl_2], as shown in Scheme 3.1. However, the catalyst tends to be less selective in the case of 3-methyl-2-cyclohexenone which undergoes further reduction to give saturated alcohol.[8]



Scheme 3.1: Example of TH of the olefinic bond of unsaturated ketones

In the same context, Selvam *et al.* reported an efficient selective hydrogenation of the C=C double bond of enones catalysed by Pd mesoporous complex with the use of ammonium carbonate as a hydrogen donor, and the desired saturated products were obtained in high yield in reaction time reaching 5 h depending on the nature of the substrates.[15] Recently, Ding *et al.* demonstrated the selective reduction of unsaturated carbonyl compounds to the corresponding saturated ones by the use of catalytic amounts of a pincer-Pd complex and under the influence of n-BuOH as a hydrogen donor (Scheme 3.2) .[16]

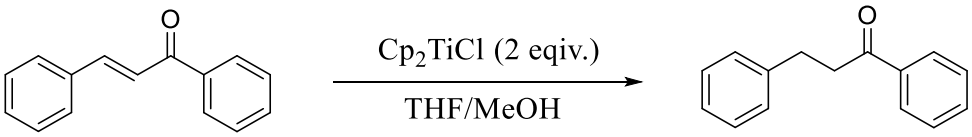


Scheme 3.2: Example of TH of the olefinic bond of unsaturated ketones

More recently, Lator *et al*. reported the use of iron complexes for the C=C selective reduction of the unsaturated ketone with the use of isopropanol or molecular hydrogen as a source of hydrogen.[17] To our knowledge, in all of the reported examples for the C=C double bond reduction of α,β-unsaturated ketones, either long reaction time, high temperature and/or inert

atmosphere is required to obtain the saturated ketone products. Furthermore, the use of methanol as a cost-effective and environmentally benign hydrogen donor and solvent for the selective TH of unsaturated ketones remains unknown. According to a report by Saburi *et al.*, the chemoselective hydrogenation of the olefinic bond was hardly proceeding when the hydrogen donor was replaced with methanol. The presence of methanol was not fruitful, providing insufficient results with regards to reactivity and decreased conversion (15%).[18] The earliest example of the use of methanol as a source of hydrogen in the C=C selective reduction of unsaturated carbonyl was disclosed in the mid of the 1980s by Maitlis *et al.*, when they used a variety of rhodium, iridium, ruthenium, and osmium complexes for 18 h at 150 ºC. However, the highest yield obtained under the optimized reaction condition was about 12%.[19]

Moisan *et al.* reported the selective reduction of olefinic bond with the use of anhydrous methanol as a hydrogen source. Nevertheless, the reduction involved the use of stoichiometric amounts of Cp_2TiCl in the presence of Zn dust as in THF at -25 ºC as shown in Scheme 3.3. Moreover, a dimerized co-product was formed along with the saturated product.[10]



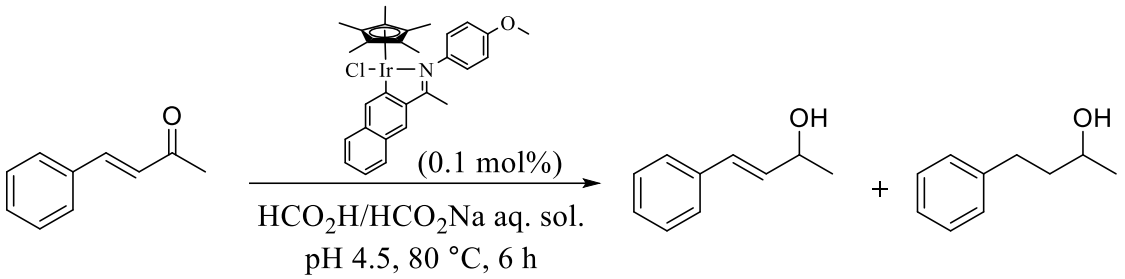
Scheme 3.3: Example of TH of the olefinic bond of unsaturated ketones

Indeed up to date, there is no catalytic system that has been reported with satisfactory performance for the selective reduction of the olefinic bond of unsaturated ketones when methanol is used as a hydrogen donor and solvent. Herein, we report that the rhodium complex **A**$_7$ (Chapter 2) is an operationally simple catalyst for selective reduction of α,β-unsaturated ketones under mild reaction conditions. The protocol involves the use of methanol as both the reaction solvent as well as hydrogen donor.

3.2 Results and discussion

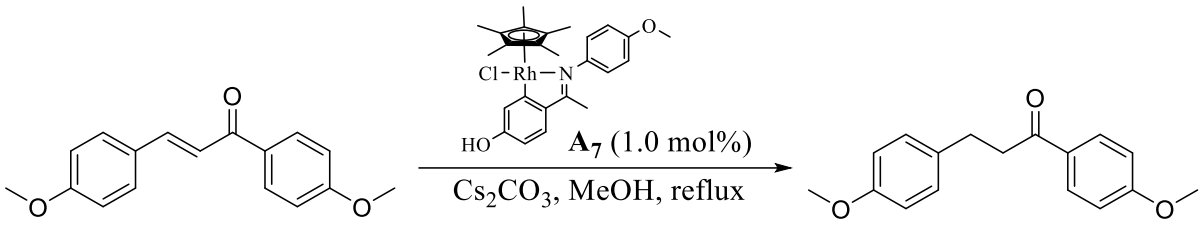
3.2.1 Optimisation of reaction conditions

Based on the successful results obtained in Chapter 2 for the TH of aldehydes with methanol, we became interested in adopting the catalyst for the reduction of more complicated systems, such as α,β-unsaturated ketones. As reported recently by Talwar *et al.*, the reduction of unsaturated ketones in an aqueous medium with an iridicycle catalyst resulted in a mixture of almost 1:1 ratio of both saturated and unsaturated alcohol as shown in Scheme 3.4.[20]



Scheme 3.4: Example of TH of α,β-unsaturated ketones with an iridicycle catalyst

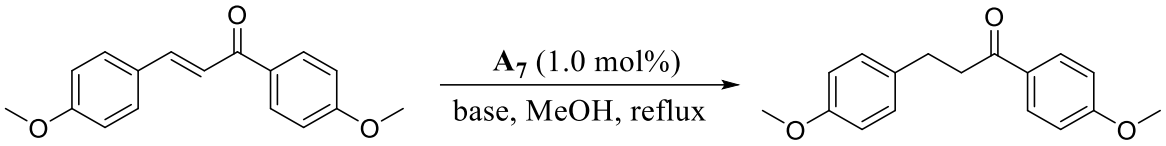
In this study, to test the feasibility of TH with the complex **A**$_7$, 4,4'-dimethoxy chalcone was chosen as a model substrate for reduction. According to what was reported, we would have three possibilities, that is either the catalyst would give a mixture of products as reported with iridium complex, or selectively reduce the carbonyl or the olefin, or both groups would be reduced to form the saturated alcohol.[20,21] To address these expectations, we subjected our reaction conditions established in Chapter 2 to the model substrate as shown in Table 3.1. Surprisingly, unlike what was reported, no reduction of the carbonyl group was observed and the reaction produced only the saturated ketone, in which the C=C double bond was reduced indicating high functional group selectivity (Scheme 3.5).



Scheme 3.5: TH of 4,4'-dimethoxy chalcone with complex **A**$_7$

After that, and in order to understand the role of the base, we examined the effect of different bases on the reduction of 4,4'-dimethoxy chalcone as shown in Table 3.1.

Table 3.1: Screening of base for the reduction of 4,4'-dimethoxy chalcone



Entry[a]	Base	Base (equiv.)	Conversion %[b]
1	Cs_2CO_3	0.5	100
2	Cs_2CO_3	0.1	50
3	Cs_2CO_3	0.25	100
4	K_2CO_3	0.25	100
5	Na_2CO_3	0.25	100
6	$CdCO_3$	0.25	40
7	NaOAc	0.25	20
8	-	-	0

[a] Reaction conditions: aldehyde (0.3 mmol), catalyst **A**$_7$ (0.003 mmol), base (equiv.) and solvent (1.5 mL), stirred at 90 °C for 1 h. [b] Determined by ^{1}H-NMR.

Variation of the type and concentration of base revealed a significant effect on the conversion. In the absence of base, no reaction is observed, which demonstrates the important role of the base in triggering the catalysed reduction (Table 3.1, Entries 1 and 8). Screening the base loading shows that the use of 0.1 equiv. was not beneficial, which lowered the conversion to 50% (Table 3.1, Entry 2), while the optimal base loading was found to be 0.25 equiv. in which a complete conversion was achieved (Table 3.1, Entry 3). The use of sodium or potassium carbonate was found to produce complete conversion in 1 hour, (Table 3.1, Entries 4 and 5). For the rest of bases, the reaction seems to be slower and the results show a clear decrease in conversion (Table 3.1, Entries 6 and 7). Based on the screening of base, K_2CO_3 was chosen to broaden the substrate scope.

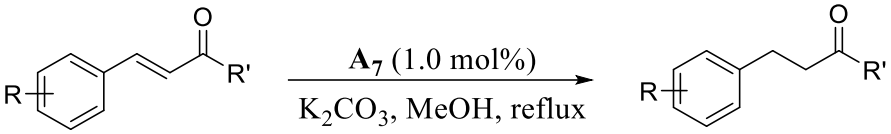
3.2.2 Transfer hydrogenation of C=C double bond of α,β-unsaturated ketones

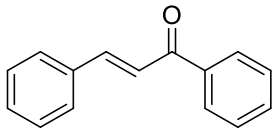
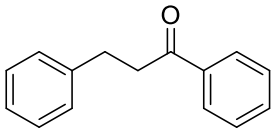
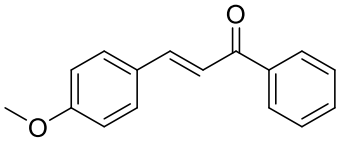
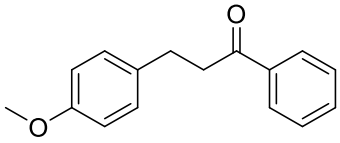
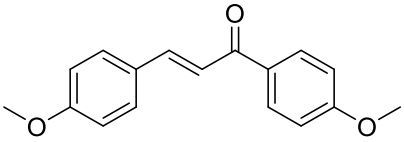
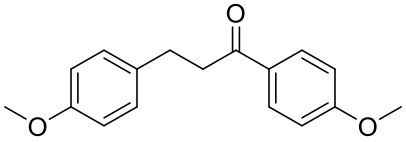
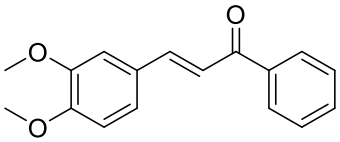
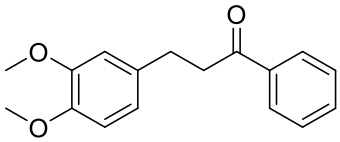
Using the above-optimized reaction conditions, this reduction system was applied to the selective reduction of C=C double bond of a range of α,β-unsaturated ketones. The results of the reduction are shown in Table 3.2. In general, the designed catalytic system has the ability to selectively reduce the vast majority of α,β-unsaturated ketones to the corresponding saturated ketone products. The isolated yield was found to be between (60- 97%) depending on the nature and position of substituents. Substituents that are electron-donating such as -OH and -OCH_3 (Table 3.2, Entries 5, 7, 8, 11, 12, 14, 15, 18, 21, 23 and 28), and electron-withdrawing, such as -Br and -Cl (Table 3.2, Entries 6, 10, 13, 16, 17, 19, 20 and 22), on the phenyl rings of the substrates, have no observed effect on the product yields under the conditions employed. Also, the introduction of electron-withdrawing substituents, such as -Br and -Cl and methyl acetate on the aromatic ring which is next to the C=C double bond, has no

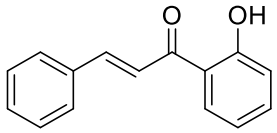
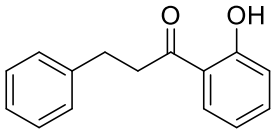
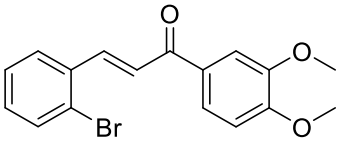
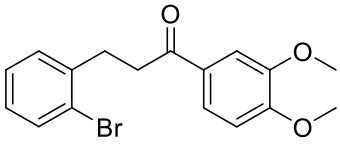
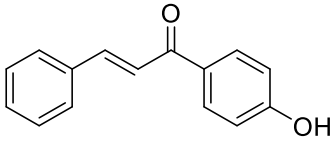
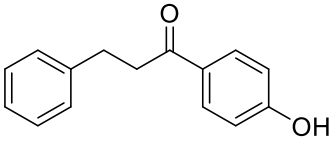
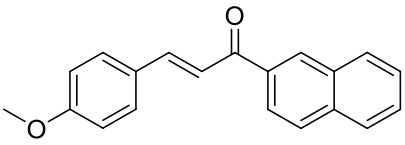
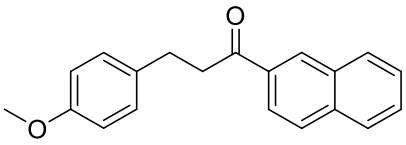
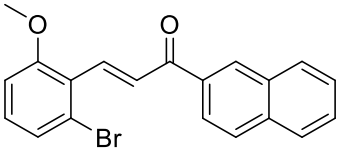
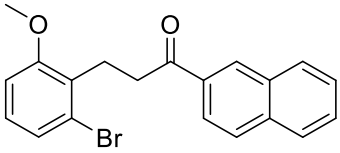
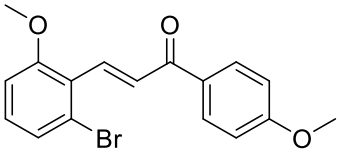
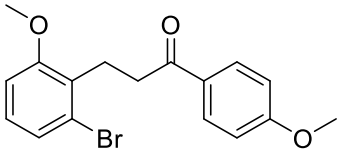
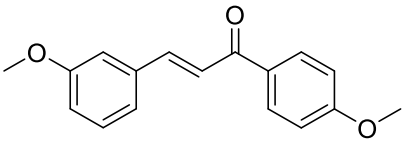
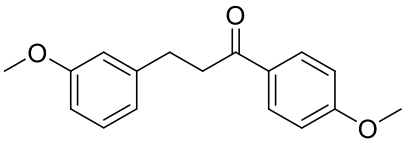
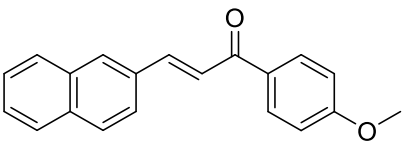
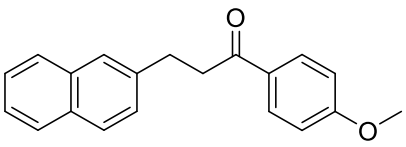
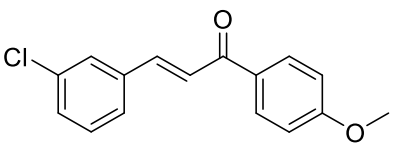
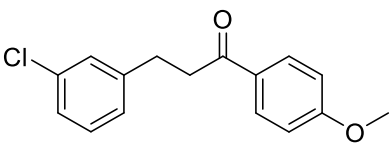
effect on the desired product and resulted in good to excellent yields (Table 3.2, Entries 6, 9, 10, 13, 16, 17, 19, 20 and 22).

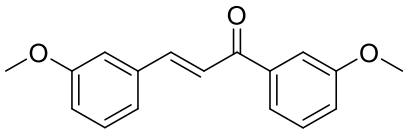
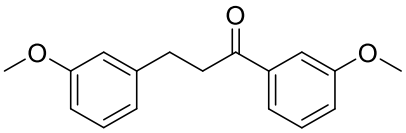
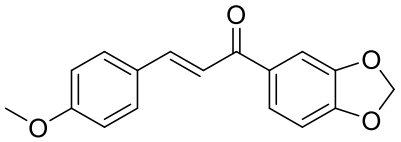
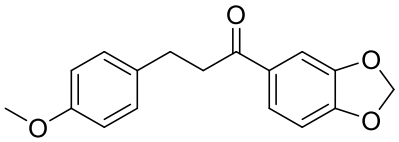
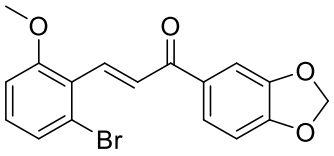
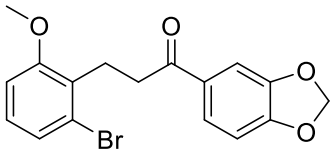
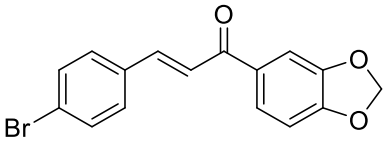
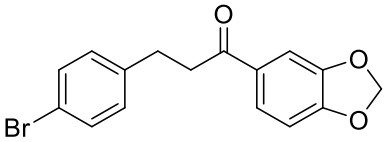
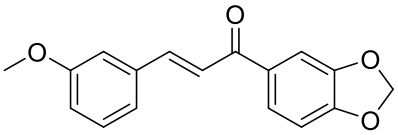
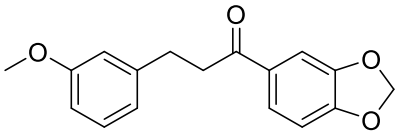
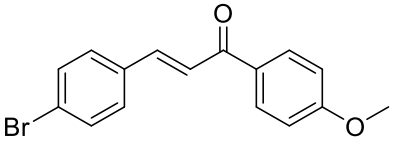
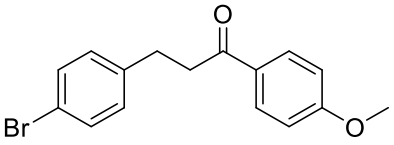
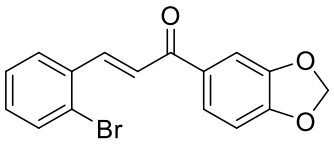
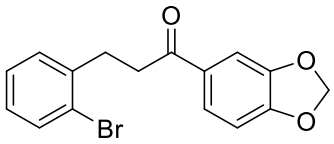
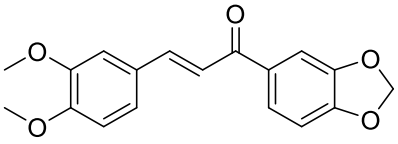
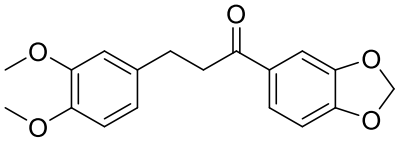
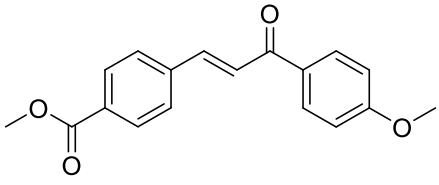
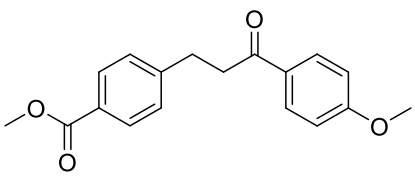
Apart from chalcones, benzylideneacetone type substrates were also viable, affording the saturated ketones in high yields (Table 3.2, Entries 23-28). Of particular note is that 2,6-disubstituted chalcones and benzylideneacetones (Table 3.2, Entries 9, 16, 26 and 27) were readily reduced, revealing no decrease in the product yield.

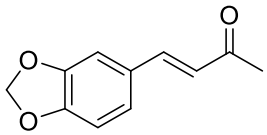
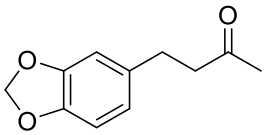
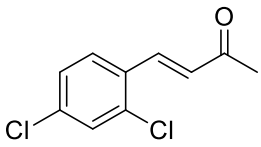
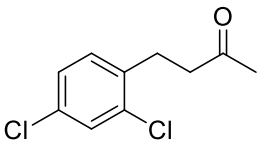
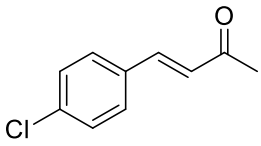
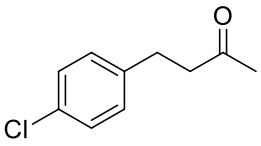
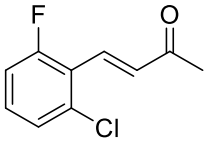
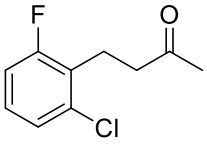
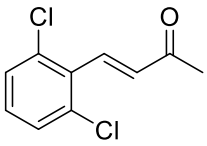
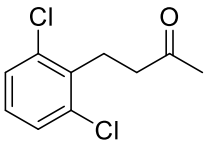
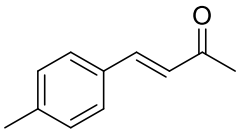
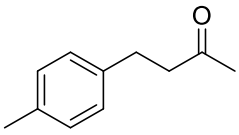
Table 3.2: Substrate scope for the reduction of unsaturated ketones with methanol



Entry[a]	Substrate	Product	Yield %[b]
1			90
2			91
3			94
4			92

5			86
6			95
7			60
8			90
9			86
10			96
11			92
12			75
13			94

14			89
15			90
16			91
17			92
18			90
19			96
20			88
21			91
22			97

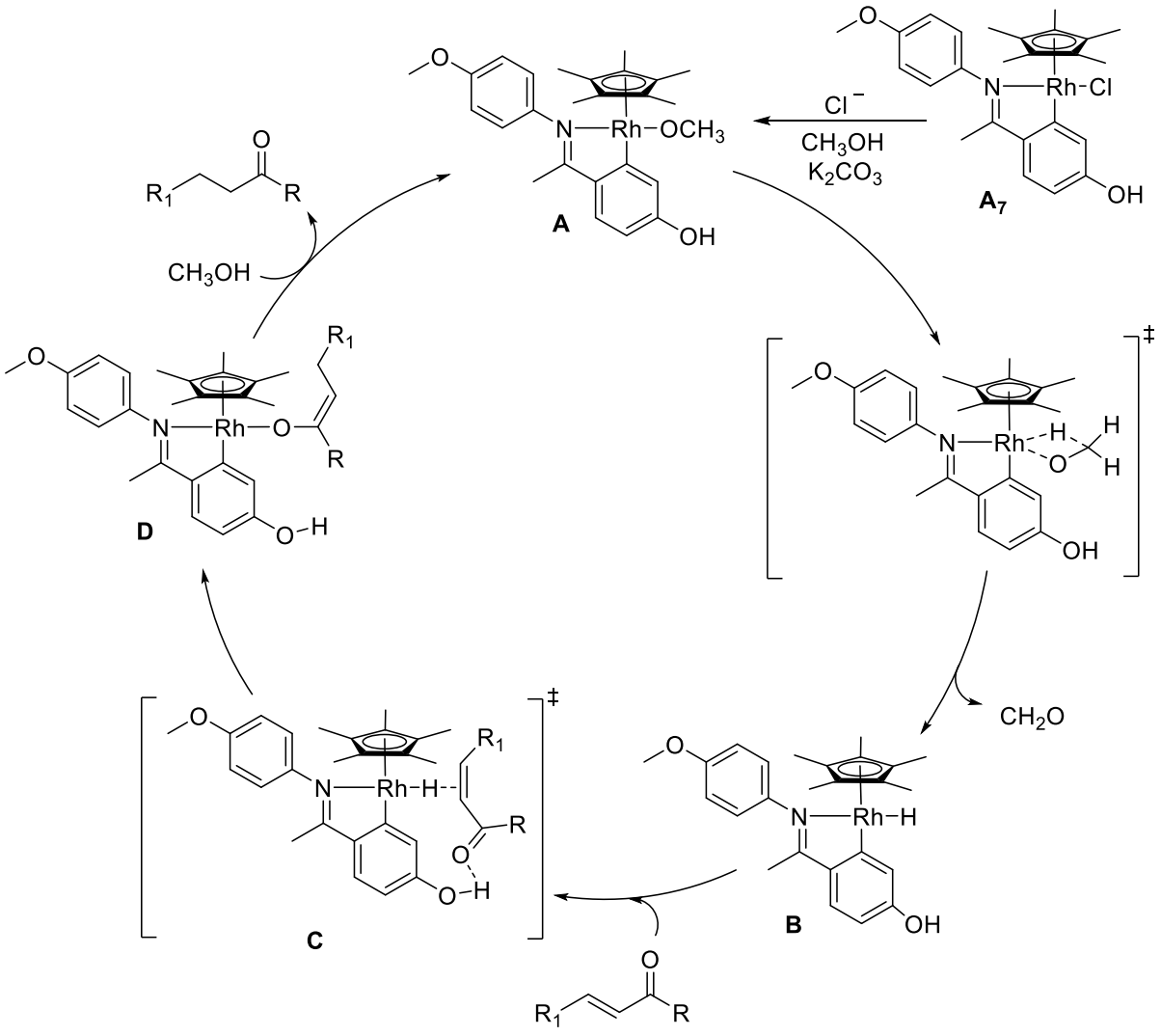
23			78
24			83
25			85
26			81
27			86
28			84

[a] Reaction conditions: aldehyde (0.3 mmol), catalyst **A**$_7$ (0.003 mmol), K_2CO_3 (0.075 mmol) and solvent (1.5 mL), stirred at 90 ºC for 1 h. [b] Yield determined by isolated product.

3.2.3 Mechanistic considerations

On the basis of the mechanism presented in Chapter 2, a simplified, plausible catalytic cycle for the selective reduction of unsaturated ketones with methanol is proposed in Scheme 3.6. The formation of the active catalyst species **A** is most likely to occur, due to the treatment of rhodium catalyst **A**$_7$ with methanol under basic condition. Then complex **A** releases H_2CO by β-hydrogen elimination via the transition state shown to form the active Rh-H species **B**. In the next step, complex **B** delivers the hydride to the C=C double bond of the unsaturated ketone

via species **C** affording the alkoxide complex **D**. Finally, complex **D** is protonated by methanol to produce the corresponding saturated ketone, regenerating the initial complex **A** for the next cycle. It is likely that the hydroxyl group of the ligand could be involved in the reduction process, facilitating the delivery of hydride to the substrate as shown in **C.** The progress of the model reaction was monitored with the passage of time (overnight) to identify possible reaction intermediates formed during the course of reaction. However, the presence of allylic alcohols or saturated alcohols was not observed at all, which indicates that catalyst selectively reduces the C=C double bond of α,β-unsaturated ketone according to Scheme 3.5.



Scheme 3.6: Plausible catalytic cycle for the selective TH of unsaturated ketones

3.3 Conclusion

In summary, exploiting the beneficial role of economic, safe, and easy-to-handle methanol that can be used as a reaction solvent and source of hydrogen, this chapter successfully shows a simple and efficient catalytic system for the selective C=C double bond TH of α,β-unsaturated ketones with broad substrate scope. This new protocol is considered the first homogeneous example that can afford highly selective hydrogenation of α,β-unsaturated ketones with methanol under mild and aerobic conditions with no need for the use of co-solvents.

3.4 Experimental and analytical data

3.4.1 General information

Unless otherwise specified, all experiments were carried out under ambient atmosphere using standard techniques. Chemicals, reagents and solvents were purchased commercially and used as received. Substrates (chalcones) were prepared by aldol condensation according to the literature method.[22] Methanol and ethanol were HPLC grade. TLC silica gel 60F254 (Merck) plates were used for the analytical thin-layer chromatography and they were revealed under ultra-violet irradiation, potassium permanganate or iodine. Columns were run using a mixture of hexane/ethyl acetate and silica gel 60 Å (230-400 mesh). ^{1}H-NMR and ^{13}C-NMR spectra were recorded on Bruker 400 MHz spectrometer using $CDCl_3$ as a solvent with TMS as the internal standard at 25 ºC. Processing and interpretation were performed with ACD- labs 12.0 (Advanced Chemistry Development Inc.). The multiplicity of the signals is abbreviated as bs (broad singlet), s (singlet), d (doublet), dd (doublets of doublet), ddd (doublet of doublet of doublet), td (triplets of doublet), p (pentet) or m (multiplet). High-resolution mass spectrum was taken by chemical ionisation (CI) at the Analytical Services of the Department of Chemistry, University of Liverpool. ^{1}H-NMR, ^{13}C-NMR and HRMS for all the products were collected, and the NMR data are consistent with the reported literature.

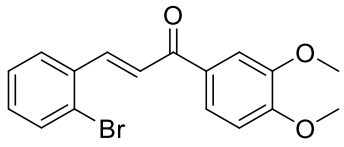
3.4.2 General procedure for chalcone synthesis

Chalcones were prepared according to the literature.[22] In a 50 mL flask equipped with a magnetic stirring bar, an acetophenone derivative (2.5 mmol) and a benzaldehyde derivative (2.5 mmol) were dissolved in absolute ethanol (10 mL). The mixture was cooled to 5 °C and then an alcoholic NaOH 40% solution (2.5 mL) was added dropwise. The reaction mixture was allowed to stir at this temperature (5 ºC) for 1 h, which was then continued at room temperature for 4 h. After that an ice-water solution was added to the reaction mixture to precipitate the product. Then the solid was filtered off with a Buchner funnel, washed with cold water and recrystallized from aqueous ethanol.

3.4.3 General procedure for the TH of unsaturated ketones in methanol

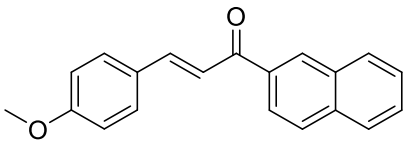
A Radleys tube was charged with unsaturated ketone (0.3 mmol), catalyst (0.003 mmol) and K_2CO_3 (0.075 mmol). MeOH (1.5 mL) was introduced, and then the reaction mixture was heated to reflux at 90 ºC for 1 h. The reaction mixture was then cooled to room temperature, followed by solvent evaporation under vacuum Flash column chromatography using hexane and ethyl acetate mixture was carried out to purify the product.

3.4.4 Analytical data of chalcone products

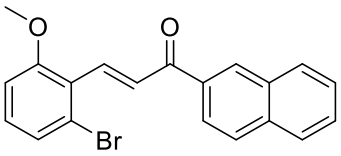


(E)-3-(2-Bromophenyl)-1-(3,4-dimethoxyphenyl)prop-2-en-1-one:[23] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 8.03 (d, J = 15.9 Hz, 1H), 7.74 (d, J = 2.3 Hz, 1H), 7.60 (d, J = 7.6 Hz, 1H), 7.55 (d, J = 15.9 Hz, 1H), 7.54 (m, 1H) 7.46 (dd, J = 8.7, 2.4 Hz, 1H), 7.41 (t, J = 7.8 Hz, 1H), 7.13 (dd, J = 8.0, 2.3 Hz, 1H), 6.82 (d, J = 8.8 Hz, 1H) 3.90 (s, 3H), 3.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 190.29, 159.88, 157.71, 139.58, 138.54, 134.03,

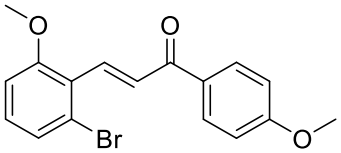
131.18, 129.57,125.96, 123.68, 121.15, 119.36, 113.04, 112.99, 112.84, 55.86, 55.50; HRMS for $C_{17}H_{15}BrO_3$ $[M + H]^+$: m/z calc.: 347.0277; found: 347.0282.



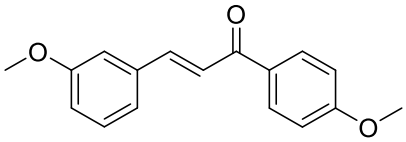
(E)-3-(4-Methoxyphenyl)-1-(naphthalen-2-yl)prop-2-en-1-one:[24] ^1H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 8.53 (s, 1H), 8.10 (dd, J = 8.5, 1.6 Hz, 1H), 8.0 (d, J = 8.0 Hz, 1H), 7.94 (d, J = 8.5 Hz, 1H), 7.90 (d, J = 8.2 Hz, 1H), 7.86 (d, J = 15.6 Hz, 1H), 7.65 (d, J = 8.5 Hz, 2H), 7.60 (t, J = 7.2 Hz, 1H), 7.58 (d, J = 15.6 Hz, 1H), 7.56 (t, J = 7.8 Hz, 1H), 6.95 (d, J = 8.6 Hz, 2H), 3.86 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 190.36, 161.71, 144,68, 135.85, 135.41, 132.60, 130.31, 129.73, 128.51, 128.27, 127.83, 126.74, 124.56, 119.79, 114.45, 55.44; HRMS for $C_{20}H_{16}O_2$ $[M + H]^+$: m/z calc.: 289.1223; found: 289.1236.



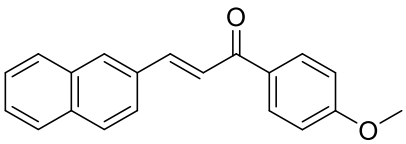
(E)-3-(2-Bromo-6-methoxyphenyl)-1-(naphthalen-2-yl)prop-2-en-1-one: ^1H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 8.54 (s, 1H), 8.11 (d, J = 15.9 Hz, 1H), 8.10 (dd, J = 8.6, 1.6 Hz, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.95 (d, J = 8.5 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.81 (d, J = 2.4 Hz, 1H), 7.72 (d, J = 15.9 Hz, 1H), 7.63-7.60 (m, 1H), 7.59-7.55 (m, 1H), 7.48 (dd, J = 8.6, 2.4 Hz, 1H), 6.84 (d, J = 8.8 Hz, 1H), 3.91 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 190.32, 157.72, 138.42, 135.54, 135.50, 134.05, 132.58, 131.05, 130.04, 129.58, 128.58, 128.40, 127.83, 126.78, 126.06, 124.55, 123.61, 113.06, 113.03, 55.89; HRMS for $C_{20}H_{15}BrO_2$ $[M + H]^+$: m/z calc.: 367.0328; found: 367.0342.



(E)-3-(2-Bromo-6-methoxyphenyl)-1-(4-methoxyphenyl)prop-2-en-1-one: ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 8.04 (d, J = 8.7 Hz, 2H), 8.02 (d, J = 15.6 Hz, 1H), 7.73 (d, J = 2.3 Hz, 1H), 7.58 (d, J = 15.6 Hz, 1H), 7.44 (dd, J = 8.7, 2.3 Hz, 1H), 6.98 (d, J = 8.7 Hz, 2H), 6.81 (d, J = 8.8 Hz, 1H), 3.88 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 188.73, 163.43, 157.62, 137.63, 133.78, 131.09, 131.04, 130.87, 126.16, 123.48, 113.84, 113.00, 112.97, 55.84, 55.50; HRMS for $C_{17}H_{15}BrO_3$ $[M + H]^+$: m/z calc.: 347.0277; found: 347.0283.

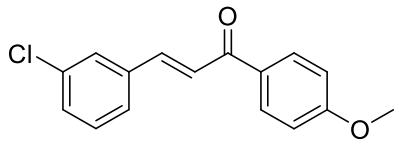


(E)-3-(3-Methoxyphenyl)-1-(4-methoxyphenyl)prop-2-en-1-one:[25] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 8.04 (d, J = 9.0 Hz, 2H), 7.76 (d, J = 15.6 Hz, 1H), 7.52 (d, J = 15.6 Hz, 1H), 7.33 (t, J = 7.9 Hz, 1H), 7.25 (d, J = 7.8 Hz, 1H), 7.15 (s, 1H), 6.99 (d, J = 8.9 Hz, 2H), 6.97-6.94 (m, 1H), 3.89 (s, 3H), 3.85 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 188.73, 163.45, 159.93, 143.89, 136.47, 131.07, 130.84, 129.92, 122.20, 121.01, 116.06, 113.86, 113.40, 55.51, 55.36; HRMS for $C_{17}H_{16}O_3$ $[M + H]^+$: m/z calc.: 269.1172; found: 269.1182.

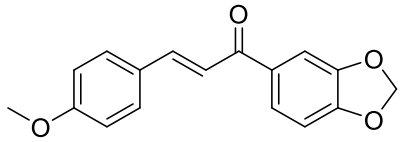


(E)-1-(4-Methoxyphenyl)-3-(naphthalen-2-yl)prop-2-en-1-one:[26] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 8.08 (d, J = 8.8 Hz, 2H), 8.01 (s, 1H), 7.96 (d, J = 15.6 Hz, 1H), 7.87-

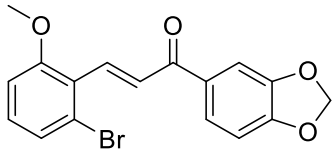
7.79 (m, 4H), 7.65 (d, J = 15.6 Hz, 1H), 7.52-7.49 (m, 2H), 6.99 (d, J = 8.8 Hz, 2H), 3.88 (s, 3H) ; ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 1.88.67, 163.45, 1.44.06, 134.31, 133.39, 132.58, 131.17, 130.86, 130.68, 128.68, 128.63, 127.81,127.28, 126.75, 123.73, 121.98, 113.88, 55.52; HRMS for $C_{20}H_{16}O_2$ $[M + H]^+$: m/z calc.: 289.1223; found: 289.1236.



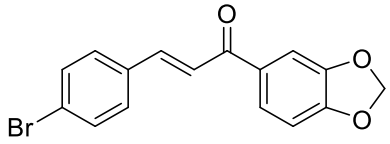
(E)-3-(3-Chlorophenyl)-1-(4-methoxyphenyl)prop-2-en-1-one:[27] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 8.04 (d, J = 8.8 Hz, 2H), 7.72 (d, J= 15.6 Hz, 1H), 7.62 (s, 1H), 7.53 (d, J= 15.6 Hz, 1H), 7.50-7.47(m, 1H), 7.35-7.34 (m, 2H), 6.99 (d, J = 8.8 Hz, 2H), 3.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 188.24, 163.62, 142.18, 136.96, 134.93, 130.88, 130.83, 130.17, 130.18, 127.79, 126.74, 123.11, 113.93, 55.52; HRMS for $C_{16}H_{13}ClO_2$ $[M + H]^+$: m/z calc.: 273.0677; found: 273.0682.



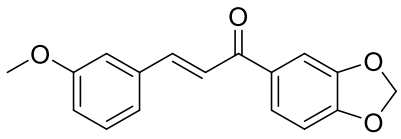
(E)-1-(Benzo[d][1,3]dioxol-5-yl)-3-(4-methoxyphenyl)prop-2-en-1-one:[28] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.78 (d, J = 15.6 Hz, 1H), 7.64 (d, J = 8.2 Hz, 1H), 7.60 (d, J = 8.5 Hz, 2H), 7.52 (s, 1H), 7.37 (d, J = 15.6 Hz, 1H), 6.94 (d, J = 8.5 Hz, 2H), 6.89 (d, J = 8.2 Hz, 1H), 6.06 (s, 2H), 3.85 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 161.58, 157.99, 151.52, 148.24, 144.11, 133.27, 130.13, 127.74, 124.47, 119.42, 114.41, 108.74, 108.45, 101.81, 55.41; HRMS for $C_{17}H_{14}O_4$ $[M + H]^+$: m/z calc.: 283.0965; found: 283.0966.



(E)-1-(Benzo[d][1,3]dioxol-5-yl)-3-(2-bromo-6-methoxyphenyl)prop-2-en-1-one: ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 8.01 (d, J = 15.8 Hz, 1H), 7.73 (d, J = 2.2 Hz, 1H), 7.65 (dd, J = 8.2, 1.2 Hz, 1H), 7.54-7.53 (m, 1H), 7.52 (d, J = 15.8 Hz, 1H), 7.45 (dd, J = 8.7, 2.2 Hz, 1H), 6.90 (d, J = 8.1 Hz, 1H), 6.82 (d, J = 8.7 Hz, 1H), 6.06 (s, 2H), 3.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 188.30, 157.66, 151.71, 148.30, 137.94, 133.85, 133.01, 131.12, 126.11, 124.76, 123.38, 112.99, 108.48, 107.91, 101.86, 55.86; HRMS for $C_{17}H_{13}BrO_4$ $[M + H]^+$: m/z calc.: 361.007; found: 361.0075.

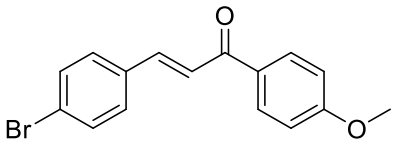


(E)-1-(Benzo[d][1,3]dioxol-5-yl)-3-(4-bromophenyl)prop-2-en-1-one:[29] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.72 (d, J = 15.6 Hz, 1H), 7.64 (dd, J = 8.0, 1.6 Hz, 1H), 7.56-7.48 (m, 5H), 7.48 (d, J = 15.6 Hz, 1H), 6.90 (d, J = 8.1 Hz, 1H), 6.07 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 187.95, 151.86, 148.23, 142.78, 133.93, 132.81, 132.19, 129.72, 124.74, 122.25, 108.42, 107.95, 101.92; HRMS for $C_{16}H_{11}BrO_3$ $[M + H]^+$: m/z calc.: 330.9964; found: 330.9962.

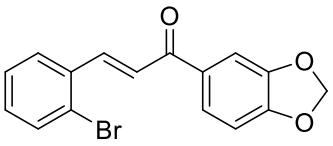


(E)-1-(Benzo[d][1,3]dioxol-5-yl)-3-(3-methoxyphenyl)prop-2-en-1-one: ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.76 (d, J = 15.6 Hz, 1H), 7.65 (dd, J = 8.2, 1.5 Hz, 1H), 7.53 (d, J = 1.5 Hz, 1H), 7.47 (d, J = 15.6 Hz, 1H), 7.33 (t, J = 7.9 Hz, 1H), 7.23 (d, J = 7.6 Hz, 1H), 7.14

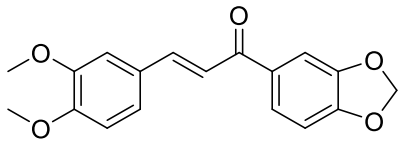
(s, 1H) 6.96 (dd, J = 8.1, 2.4 Hz, 1H), 7.90 (d, J = 8.1 Hz, 1H), 6.06 (s, 2H), 3.86 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 188.26, 159.96, 151.73, 148.32, 144.16, 136.39, 132.97, 129.92, 124.70, 122.05, 121.02, 116.16, 113.40, 108.46, 107.93, 101.88, 55.36; HRMS for $C_{17}H_{14}O_4$ $[M + H]^+$: m/z calc.: 283.0965; found: 283.0973.



(E)-3-(4-Bromophenyl)-1-(4-methoxyphenyl)prop-2-en-1-one:[30] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 8.03 (d, J = 8.8 Hz, 2H), 7.73 (d, J = 15.6 Hz, 1H), 7.56-7.49 (m, 5H), 6.99 (d, J = 8.8 Hz, 2H), 3.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 188.39, 163.57, 142.50, 134.03, 132.17, 130.93, 130.84, 129.71, 124.53, 122.42, 113.91, 55.52; HRMS for $C_{16}H_{13}BrO_2$ $[M + H]^+$: m/z calc.: 317.0172; found: 317.0175.

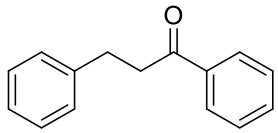


(E)-1-(Benzo[d][1,3]dioxol-5-yl)-3-(2-bromophenyl)prop-2-en-1-one:[31] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 8.10 (d, J = 15.7 Hz, 1H), 7.72 (dd, J = 7.7, 0.8 Hz, 1H), 7.64 (m, 2H), 7.53 (d, J = 1.2 Hz, 1H), 7.39 (d, J = 15.6 Hz, 1H), 7.35 (t, J = 7.6 Hz, 1H), 7.24 (m, 1H), 6.90 (d, J = 8.2 Hz, 1H) 6.07 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 188.13, 151.86, 148.37, 142.59, 135.22, 133.55, 132.69, 131.18, 127.86, 127.67, 125.80, 124.93, 124.81, 108.52, 107.93, 101.91; HRMS for $C_{16}H_{11}BrO_2$ $[M + H]^+$: m/z calc.: 330.9964; found: 330.09971.

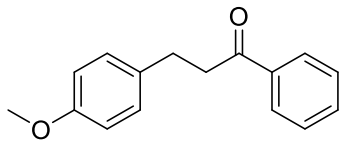


(E)-1-(Benzo[d][1,3]dioxol-5-yl)-3-(3,4-dimethoxyphenyl)prop-2-en-1-one: ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.75 (d, J = 15.5 Hz, 1H), 7.65 (d, J = 8.1 Hz, 1H), 7.53 (s, 1H), 7.35 (d, J = 15.5 Hz, 1H), 7.22 (d, J = 8.2 Hz, 1H), 7.15 (s, 1H), 6.90 (d, J = 8.2 Hz, 2H), 6.06 (s, 2H), 3.95 (s, 3H), 3.93 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 188.31, 151.54, 151.35, 149.26, 148.24, 144.43, 133.23, 127.99, 124.50, 123.05, 119.66, 111.14, 110.07, 108.46, 107.90, 101.83, 56.01, 55.99; HRMS for $C_{18}H_{16}O_5$ $[M + H]^+$: m/z calc.: 313.1071; found: 313.1081.

3.4.5 Analytical data of saturated ketones products

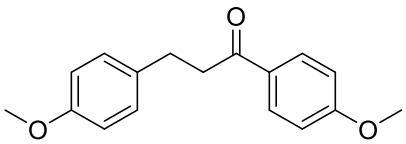


1,3-Diphenylpropan-1-one:[32] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.96 (d, J = 7.6 Hz, 2H), 7.55 (t, J = 7.5 Hz, 1H), 7.45 (t, J = 7.4 Hz, 2H), 7.31-7.28 (m, 2H), 7.25-7.18 (m, 3H), 3.30 (t, J = 8.0 Hz, 2H), 3.07 (t, J = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 199.23, 141.30, 136.87, 133.06, 128.5, 128.61, 128.53, 128.43, 128.04, 126.14, 40.45, 30.14; HRMS for $C_{15}H_{14}O$ $[M + H]^+$: m/z calc.: 211.1117; found: 211.1126.

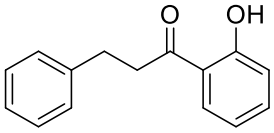


3-(4-Methoxyphenyl)-1-phenyl-1-propanone:[33] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): δ 7.95 (d, J = 7.3 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.8 Hz, 2H), 7.17 (d, J = 8.3 Hz, 2H), 6.84 (d, J = 8.5 Hz, 2H), 3.78 (s, 3H), 3.26 (t, J = 8.0 Hz, 2H), 3.01 (t, J = 7.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 199.4, 158.0, 136.92, 133.33, 133.03,

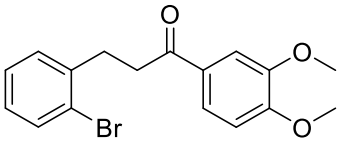
129.36, 128.6, 128.05, 113.95, 55.28, 40.71, 29.29.; HRMS for $C_{16}H_{16}O_2$ $[M + H]^+$: m/z calc.: 241.1223; found: 241.1225.



1,3-Bis(4-methoxyphenyl)-1-propanone:[34] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): δ 7.93 (d, J = 8.8 Hz, 2H), 7.17 (d, J = 8.7 Hz, 2H), 6.92 (d, J = 8.9 Hz, 2H), 6.84 (d, J = 8.7 Hz, 2H), 3.86 (s, 3H), 3.78 (s, 3H), 3.21 (t, J = 7.2 Hz, 2H), 2.99 (t, J = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 197.99, 163.44, 157.97, 133.49, 130.31, 130.02, 129.35, 113.92, 113.72, 55.46, 55.27, 40.37, 29.49; HRMS for $C_{17}H_{18}O_3$ $[M + H]^+$: m/z calc.: 271.1329; found: 271.1335.

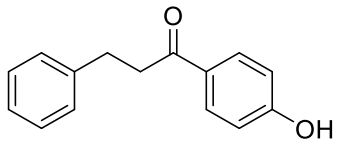


1-(2-Hydroxyphenyl)-3-phenyl-1-propanone:[35] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 12.29 (s, 1H, OH), 7.74 (dd, J = 8.1, 1.4 Hz, 1H), 7.45-7.43 (m, 1H), 7.32-7.28 (m, 2H), 7.25-7.21 (m, 3H), 6.98 (dd, J = 8.3, 0.88 Hz, 1H), 6.87 (td, J = 8.0, 1.1 Hz, 1H), 3.32 (t, J = 7.3 Hz, 2H), 3.00 (t, J = 7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 205.39, 162.49, 140.73, 136.36, 129.83, 128.62, 128.40, 126.33, 119.29, 118.93, 118.58, 40.05, 30.04; HRMS for $C_{15}H_{14}O_2$ $[M + H]^+$: m/z calc.: 227.1067; found: 227.1076.

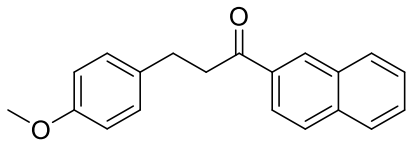


3-(2-Bromophenyl)-1-(3,4-dimethoxyphenyl)-1-propanone: ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.54 (d, J = 7.6 Hz, 1H), 7.49-7.48 (m, 1H), 7.34 (t, J = 7.9 Hz, 1H), 7.30-7.27

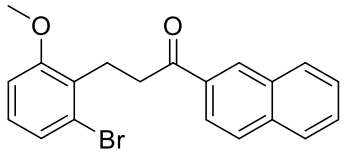
(m, 2H), 7.09 (dd, J = 8.2, 1.8 Hz, 1H), 6.71 (d, J = 8.5 Hz, 1H), 3.84 (s, 3H), 3.79 (s, 3H), 3.21 (t, J = 7.2 Hz, 2H), 2.99 (t, J = 8.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 199.21, 159.84, 156.66, 138.23, 132.78, 131.88, 130.06, 129.54, 120.70, 119.45, 112.62, 112.38, 111.92, 55.45, 38.64, 25.38; HRMS for $C_{17}H_{17}BrO_3$ $[M + H]^+$: m/z calc.: 349.0434; found: 349.0443.



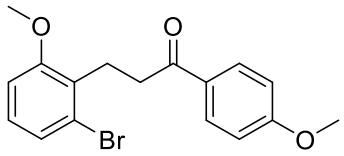
1-(4-Hydroxyphenyl)-3-phenylpropan-1-one:[36] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.89 (d, J = 8.8 Hz, 2H), 7.30-7.19 (m, 5H), 6.89 (d, J = 8.6 Hz, 2H), 3.25 (t, J = 7.2 Hz, 2H), 3.04 (t, J = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 199.03, 160.76, 141.20, 131.81, 129.60, 128.55, 128.40, 126.16, 115.50, 40.13, 30.47; HRMS for $C_{15}H_{14}O_2$ $[M + H]^+$: m/z calc.: 227.1067; found: 227.1078.



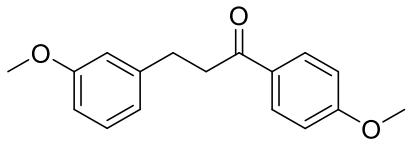
3-(4-Methoxyphenyl)-1-(naphthalen-2-yl)propan-1-one:[37] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 8.43 (s, 1H), 8.02 (dd, J = 8.6, 1.7 Hz, 1H), 7.92 (d, J = 7.8 Hz, 1H), 7.85 (t, J = 8.2 Hz, 2H), 7.59-7.50 (m, 2H), 7.20 (d, J = 8.6 Hz, 2H), 6.85 (d, J = 8.6 Hz, 2H), 3.77 (s, 3H), 3.39 (t, J = 7.3 Hz, 2H), 3.06 (t, J = 7.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 199.33, 158.05, 135.58, 134.25, 133.39, 132.54, 129.7, 129.56, 129.41, 128.45, 128.43, 127.78, 126.77, 123.87, 113.99, 55.29, 40.83, 29.45; HRMS for $C_{20}H_{18}O_2$ $[M + H]^+$: m/z calc.: 291.138; found: 291.1392.



3-(2-Bromo-6-methoxyphenyl)-1-(naphthalen-2-yl)propan-1-one: ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 8.46 (s, 1H), 8.04 (dd, J = 8.6, 1.7 Hz, 1H), 7.94 (d, J = 7.9 Hz, 1H), 7.87 (t, J = 8.2 Hz, 2H), 7.61-7.52 (m, 2H), 7.35 (d, J = 2.5 Hz, 1H), 7.30 (dd, J = 8.5, 2.5 Hz, 1H), 6.73 (d, J = 8.6 Hz, 1H), 3.81 (s, 3H), 3.36 (t, J = 7.3 Hz, 2H), 3.05 (t, J = 7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 199.35, 156.69, 135.57, 134.18, 132.81, 132.54, 131.95, 131.95, 130.09, 129.73, 129.53, 128.41, 127.79, 126.74, 123.91, 112.68, 111.96, 55.52, 38.67, 25.47; HRMS for $C_{20}H_{17}BrO_2$ $[M + H]^+$: m/z calc.: 369.0485; found: 369.0499.

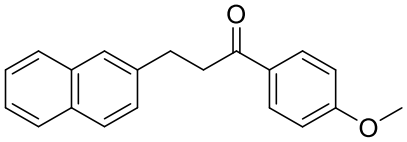


3-(2-Bromo-6-methoxyphenyl)-1-(4-methoxyphenyl)propan-1-one: ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.94 (d, J = 8.9 Hz, 2H), 7.30-7.25 (m, 2H), 6.91 (d, J = 8.9 Hz, 2H), 6.70 (d, J = 8.6 Hz, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 3.17 (t, J = 7.1 Hz, 2H), 2.99 (t, J = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 197.97, 163.40, 156.67, 132.73, 132.08, 130.32, 129.99, 129.97, 113.69, 112.61, 111.93, 55.49, 55.46, 38.19, 25.4; HRMS for $C_{17}H_{17}BrO_3$ $[M + H]^+$: m/z calc.: 349.0434; found: 349.0436.

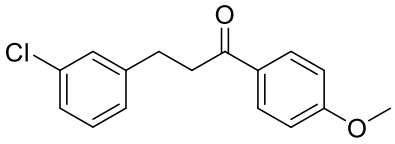


3-(3-Methoxyphenyl)-1-(4-methoxyphenyl)propan-1-one:[38] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.94 (d, J = 8.8 Hz, 2H), 7.20 (t, J = 7.9 Hz, 1H), 6.92 (d, J = 8.8 Hz, 2H), 6.84 (d, J = 7.2 Hz, 1H), 6.79 (s, 1H), 6.74 (dd, J = 8.1, 2.2 Hz, 1H), 3.85 (s, 3H), 3.78 (s, 3H),

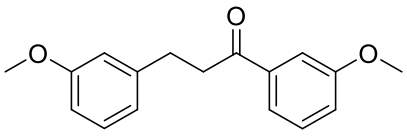
3.23 (t, J = 7.2 Hz, 2H), 3.02 (t, J = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 197.77, 163.47, 159.74, 143.12, 130.31, 129.98, 129.49, 120.78, 114.23, 113.73, 111.38, 55.46, 55.16, 40.02, 30.39; HRMS for $C_{17}H_{18}O_3$ $[M + H]^+$: m/z calc.: 271.1329; found: 271.1339.



1-(4-Methoxyphenyl)-3-(naphthalen-2-yl)propan-1-one:[38] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.96 (d, J = 8.9 Hz, 2H), 7.79 (t, J = 7.8 Hz, 3H), 7.68 (s, 1H), 7.46-7.38 (m, 3H), 6.92 (d, J = 9.0 Hz, 2H), 3.85 (s, 3H), 3.33 (t, J = 7.9 Hz, 2H), 3.21 (t, J = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 197.75, 163.47, 138.79, 133.64, 132.08, 130.33, 129.99, 128.09, 127.62, 127.46, 127.21, 126.48, 126.00, 125.28, 113.77, 55.47, 40.03, 30.48; HRMS for $C_{20}H_{18}O_2$ $[M + H]^+$: m/z calc.: 291.138; found: 291.1391.

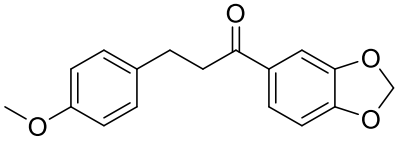


3-(3-Chlorophenyl)-1-(4-methoxyphenyl)propan-1-one:[39] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.92 (d, J = 8.9 Hz, 2H), 7.25-7.11 (m, 4H), 6.91 (d, J= 8.8 Hz, 2H), 3.84 (s, 3H), 3.22 (t, J = 7.3 Hz, 2H), 3.02 (t, J = 7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 197.24, 163.54, 143.55, 134.19, 130.29, 129.83, 129.75, 128.57, 126.72, 126.28, 113.78, 55.47, 39.63, 29.85; HRMS for $C_{16}H_{15}ClO_2$ $[M + H]^+$: m/z calc.: 275.0833; found: 275.0836.

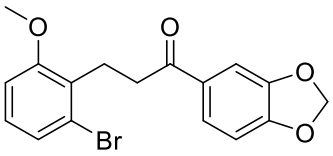


1,3-Bis(3-methoxyphenyl)-1-propanone:[40] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.52 (d, J = 7.7 Hz, 1H), 7.47 (s, 1H), 7.34 (t, J = 8.0 Hz, 1H), 7.16 (d, J = 8.5 Hz, 2H), 7.09 (dd, J

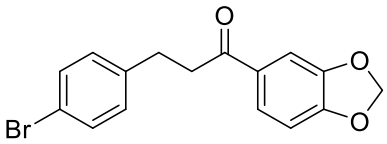
= 8.2, 2.4 Hz, 1H), 6.84 (d, J = 8.5 Hz, 2H), 3.84 (s, 3H), 3.78 (s, 3H), 3.24 (t, J = 7.8 Hz, 2H), 3.00 (t, J = 7.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 199.20, 159.85, 158.01, 138.30, 133.29, 129.57, 129.36, 120.68, 119.54, 113.95, 112.27, 55.44, 55.27, 40.82, 29.35; HRMS for $C_{17}H_{18}O_3$ $[M + H]^+$: m/z calc.: 271.1329; found: 271.1321.



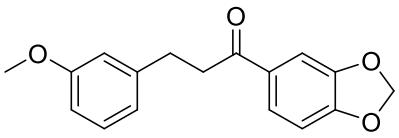
1-(Benzo[d][1,3]dioxol-5-yl)-3-(4-methoxyphenyl)-1-propanone:[41] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.54 (dd, J = 8.2, 1.6 Hz, 1H), 7.43 (d, J = 1.6 Hz, 1H), 7.15 (d, J = 8.6 Hz, 2H), 6.83 (dd, J = 8.6, 3.7 Hz, 3H), 6.02 (s, 2H), 3.78 (s, 3H), 3.17 (t, J = 7.3 Hz, 2H), 2.98 (t, J = 7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 197.44, 157.99, 151.69, 148.18, 133.36, 131.82, 129.33, 124.23, 113.93, 107.89, 107.85, 101.81, 55.27, 40.46, 29.51; HRMS for $C_{17}H_{16}O_4$ $[M + H]^+$: m/z calc.: 285.1121; found: 285.113.



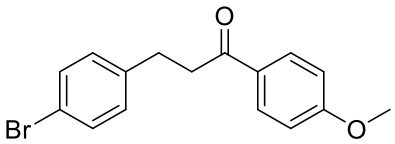
1-(1,3-Benzodioxol-5-yl)-3-(2-bromo-6-methoxyphenyl)propan-1-one: ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.56 (dd, J = 8.1, 1.5 Hz, 1H), 7.45 (s, 1H), 7.29-7.27 (m, 2H), 6.83 (d, J = 8.2 Hz, 1H), 6.72 (d, J = 8.2 Hz, 1H), 6.03 (s, 2H), 3.80 (s, 3H), 3.14 (t, J = 7.3 Hz, 2H), 2.97 (t, J = 7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 197.48, 156.64, 151.65, 148.14, 132.74, 131.93, 131.73, 130.03, 124.26, 112.63, 111.92, 107.95, 107.84, 101.80, 55.48, 38.32, 25.55; HRMS for $C_{17}H_{15}BrO_4$ $[M + H]^+$: m/z calc.: 363.0226; found: 363.0228.



1-(1,3-Benzodioxol-5-yl)-3-(4-bromophenyl)propan-1-one: ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.53 (dd, J = 8.2, 1.7 Hz, 1H), 7.42 (d, J = 1.6 Hz, 1H), 7.40 (d, J = 8.4 Hz, 2H), 7.12 (d, J = 8.4 Hz, 2H), 6.83 (d, J = 8.0 Hz, 1H), 6.03 (s, 2H), 3.19 (t, J = 7.7 Hz, 2H), 2.99 (t, J = 7.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 196.84, 151.81, 148.23, 140.30, 131.65, 131.53, 130.22, 124.23, 119.87, 107.89, 107.84, 101.86, 39.80, 29.65; HRMS for $C_{16}H_{13}BrO_3$ $[M + H]^+$: m/z calc.: 333.0121; found: 333.013.

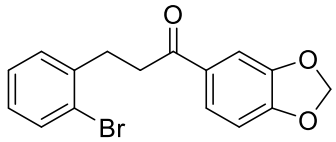


1-(1,3-Benzodioxol-5-yl)-3-(3-methoxyphenyl)propan-1-one:[41] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.56 (dd, J = 8.2, 1.7 Hz, 1H), 7.44 (d, J = 1.6 Hz, 1H), 7.20 (t, J = 7.8 Hz, 1H), 6.83 (d, J = 8.0 Hz, 2H), 6.78 (s, 1H) 6.75 (dd, J = 8.1, 2.3 Hz, 1H), 6.02 (s, 2H), 3.79 (s, 3H), 3.21 (t, J = 7.3 Hz, 2H), 3.01 (t, J = 7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 197.24, 159.74, 151.72, 148.20, 142.98, 131.76, 129.50, 124.24, 120.76, 114.22, 111.40, 107.88, 101.83, 55.17, 40.12, 30.40; HRMS for $C_{17}H_{16}O_4$ $[M + H]^+$: m/z calc.: 285.1121; found: 285.1132.

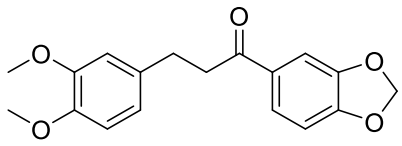


1-(4-Methoxyphenyl)-3-(4-bromophenyl)-1-propanone:[39] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.92 (d, J = 8.8 Hz, 2H), 7.39 (d, J = 8.3 Hz, 2H), 7.12 (d, J = 8.3 Hz, 2H), 6.91 (d, J = 8.8 Hz, 2H), 3.85 (s, 3H), 3.21 (t, J = 7.3 Hz, 2H), 3.00 (t, J = 7.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 197.35, 163.53, 140.46, 131.52, 130.28, 130.25, 129.86,

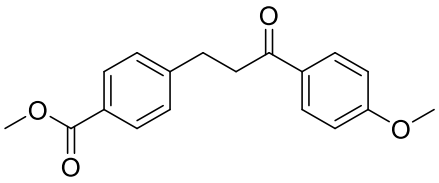
119.82, 113.77, 55.48, 39.70, 29.62; HRMS for $C_{16}H_{15}BrO_2$ $[M + H]^+$: m/z calc.: 319.0328; found: 319.0341.



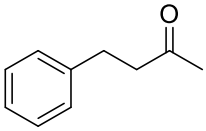
1-(Benzo[d][1,3]dioxol-5-yl)-3-(2-bromophenyl)propan-1-one:[42] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.55 (dd, J = 8.2, 1.7 Hz, 1H), 7.52 (dd, J = 8.0, 0.90 Hz, 1H), 7.44 (d, J = 1.5 Hz, 1H), 7.29 (dd, J = 7.6, 1.5 Hz, 1H), 7.22 (td, J = 7.4, 1.0 Hz, 1H), 7.06 (td, J = 7.8, 1.7 Hz, 1H), 6.81 (d, J = 8.2 Hz, 1H) 6.01 (s, 2H), 3.23-3.19 (m, 2H), 3.16-3.11 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 196.96, 151.76, 148.19, 140.61, 132.87, 131.66, 130.78, 127.97, 127.63, 124.36, 124.33, 107.88, 101.85, 38.37, 31.02; HRMS for $C_{16}H_{13}BrO_2$ $[M + H]^+$: m/z calc.: 333.0121; found: 333.0128.



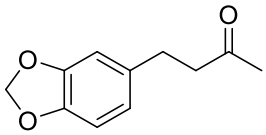
1-Benzo[1,3]dioxol-5-yl-3-(3,4-dimethoxy-phenyl)-propan-1-one: ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.55 (dd, J = 8.2, 1.7 Hz, 1H), 7.44 (d, J = 1.6 Hz, 1H), 6.83 (d, J = 8.2 Hz, 1H), 6.79 (s, 1H) 6.78-6.67 (m, 2H), 6.03 (s, 2H), 3.86 (s, 3H), 3.85 (s, 3H), 3.19 (t, J = 7.3 Hz, 2H), 2.99 (t, J = 7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 197.44, 151.72, 148.92, 148.19, 147.40, 133.95, 131.82, 124.25, 120.16, 111.85, 111.35, 107.88, 107.86, 101.83, 55.94, 55.85, 40.45, 30.04; HRMS for $C_{18}H_{18}O_5$ $[M + H]^+$: m/z calc.: 315.1227; found: 315.1237.



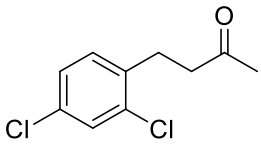
Methyl 4-(3-(4-methoxyphenyl)-3-oxopropyl)benzoate:[34] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.96 (d, J = 8.3 Hz, 2H), 7.93 (d, J = 8.9 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 3.89 (s, 3H), 3.86 (s, 3H), 3.26 (t, J = 7.8 Hz, 2H), 3.10 (t, J = 7.8 Hz, 2H);^{13}C NMR (100 MHz, $CDCl_3$) δ 197.24, 167.04, 163.55, 147.00, 130.28, 129.84, 128.49, 128.09, 113.77, 55.47, 52.00, 39.44, 30.21; HRMS for $C_{18}H_{18}O_4$ $[M + H]^+$: m/z calc.: 299.1278; found: 299.1283.



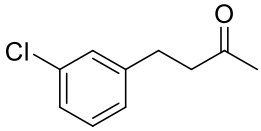
4-Phenylbutan-2-one:[43] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.29-7.25 (m, 2H), 7.20-7.17(m, 3H), 2.89 (t, J = 7.7 Hz, 2H), 2.75 (t, J = 7.7 Hz, 2H), 2.13 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.92, 140.99, 128.50, 128.29, 126.11, 45.18, 30.07, 29.74; HRMS for $C_{10}H_{12}O$ $[M + H]^+$: m/z calc.: 149.0961; found: 149.0966.



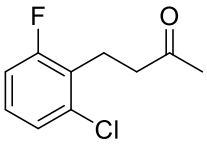
4-(Benzo[d][1,3]dioxol-5-yl)butan-2-one:[44] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 6.71 (d, J = 7.9 Hz, 1H), 6.66 (s, 1H), 6.62 (d, J = 7.9 Hz, 1H), 5.91 (s, 2H), 2.81 (t, J = 7.1 Hz, 2H), 2.70 (t, J = 7.1 Hz, 2H), 2.13 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 207.88, 147.63, 145.83, 134.79, 121.04, 108.73, 108.23, 100.82, 45.41, 30.10, 29.48; HRMS for $C_{11}H_{12}O_3$ $[M + NH_4]^+$: m/z calc.: 210.1125; found: 210.1130.



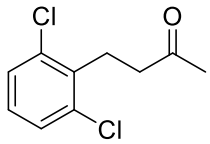
4-(2,4-Dichlorophenyl)butan-2-one:[45] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.35 (d, J = 1.7 Hz, 1H), 7.19-7.14 (m, 2H), 2.96 (t, J = 7.4 Hz, 2H), 2.74 (t, J = 7.6 Hz, 2H), 2.14 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 207.16, 137.18, 134.47, 132.62, 131.49, 129.27, 127.15, 42.90, 29.97, 27.16; HRMS for $C_{10}H_{10}Cl_2O$ $[M + H]^+$: m/z calc.: 217.0181; found: 217.0188.



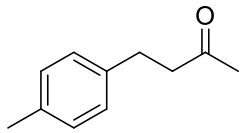
4-(2-Chlorophenyl)but-3-en-2-one:[46] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.18-7.12 (m, 3H), 6.99 (d, J = 7.1 Hz, 1H), 2.79 (t, J = 7.4 Hz, 2H), 2.67 (t, J = 7.4 Hz, 2H), 2.07 (s, 3H).; ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 207.29, 143.07, 134.21, 129.73, 128.45, 126.57, 126.32, 44.72, 30.06, 29.25; HRMS for $C_{10}H_{11}ClO$ $[M + H]^+$: m/z calc.: 183.0571; found: 183.0577.



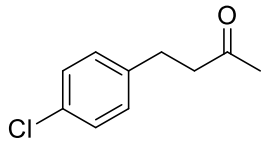
4-(2-Chloro-6-fluorophenyl)butan-2-one: ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.16-7.09 (m, 2H), 6.95 (t, J = 7.7 Hz, 1H), 3.04 (t, J = 7.7 Hz, 2H), 2.70 (t, J = 7.7 Hz, 2H), 2.18 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 207.19, 161.34 (d, J_{C-F} = 245.87 Hz), 135.04 (d, J_{C-F} = 6.13 Hz), 127.91 (d, J_{C-F} = 4.6 Hz), 126.73 (d, J_{C-F} = 22.55 Hz), 125.22 (d, J_{C-F} = 3.83 Hz), 113.94 (d, J_{C-F} = 22.9 Hz), 42.22, 29.72, 20.75 (d, J_{C-F} = 3.06 Hz); HRMS for $C_{10}H_{10}ClFO$ $[M + H]^+$: m/z calc.: 201.0477; found: 201.0483.



4-(2,6-Dichlorophenyl)butan-2-one: ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.27 (d, J = 7.9 Hz, 2H), 7.08 (t, J = 8.0 Hz, 1H), 3.18 (t, J = 8.1 Hz, 2H), 2.69 (t, J = 8.1 Hz, 2H), 2.20 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 207.22, 136.80, 135.25, 128.20, 127.90, 41.42, 29.73, 25.57; HRMS for $C_{10}H_{10}Cl_2O$ $[M + H]^+$: m/z calc.: 217.0181; found: 217.0191.



4-(p-tolyl)butan-2-one:[44] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.09-7.05 (m, 4H), 2.84 (t, J = 7.7, 2H), 2.72 (t, J = 7.6, 2H), 2.30 (s, 3H), 2.12 (s, 3H) ; ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 208.06, 137.90, 135.59, 129.18, 128.17, 45.33, 30.07, 29.35, 20.99; HRMS for $C_{11}H_{14}O$ $[M + NH_4]^+$: m/z calc.: 180.1383; found: 180.1388.



4-(4-Chlorophenyl)but-3-en-2-one:[43] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.24 (d, J = 8.2 Hz, 2H), 7.11 (d, J = 8.2 Hz, 2H), 2.85 (t, J = 7.4 Hz, 2H), 2.73 (t, J = 7.4 Hz, 2H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.45, 139.48, 131.85, 129.69, 128.57, 44.89, 30.08, 28.98; HRMS for $C_{10}H_{11}ClO$ $[M + H]^+$: m/z calc.: 183.0571; found: 183.0576.

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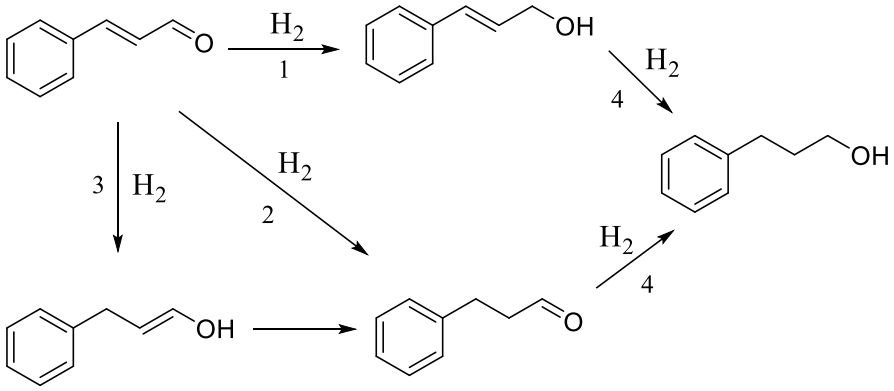
Chapter 4

Room temperature reduction of α,β-unsaturated aldehyde with methanol

4.1 Introduction

The hydrogenation reactions of α,β-unsaturated aldehydes are a valuable transformation that are widely used in the preparation of a large number of fine chemicals, particularly in the field of pharmaceutical, fragrance and flavour chemistry.[1–3] Obviously, the great demand for the hydrogenation of such system comes from the various products that could be achieved from their reduction reaction. For example, the hydrogenation of cinnamaldehyde can proceed in four different pathways giving three different products, as shown in Scheme 4.1. The first path involves the 1,2-hydrogen addition to the cinnamaldehyde to form the unsaturated alcohol (1), while in the second path the cinnamaldehyde undergoes the 3,4-addition to produce the saturated aldehyde (2). The third path gives the enol product by the 1,4-addition which is subsequently converted into the saturated aldehyde (3). The final path will result in the formation of the saturated alcohol through the hydrogenation of both C=C and C=O groups (4).[4,5]



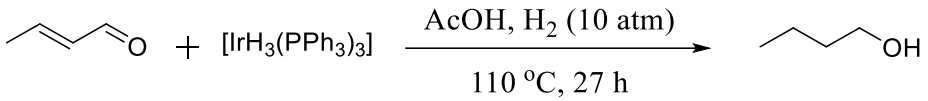
Scheme 4.1: The hydrogenation reaction of α,β-unsaturated aldehydes

Usually, the reduction of α,β-unsaturated aldehydes is carried out with stoichiometric amounts of metal hydrides such as sodium borohydride or lithium aluminium hydride. However, this type of reagents produces a stoichiometric amount of by-products and generates solid waste, which is environmentally unfavourable. In comparison, the homogeneous or heterogeneous

catalytic hydrogenation with H_2 is undoubtedly more preferred and can be considered environmentally acceptable because it does not form any by-products.[2,6]

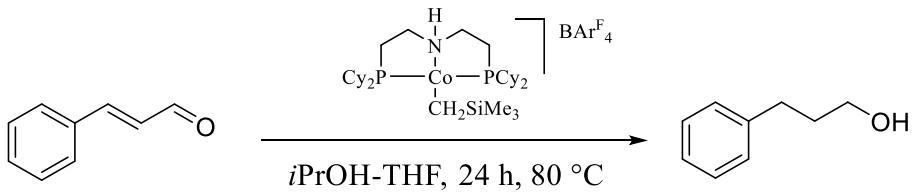
Reducing the carbonyl group of α,β-unsaturated aldehydes selectively to saturated alcohol is usually achieved with relative ease. In contrast, the selective reduction of the olefinic bond over carbonyl groups has been quite challenging and remains limited.[7]

Early efforts into the reduction of α,β-unsaturated aldehydes, were reported by Strohmeier *et al.* for the hydrogenation of crotonaldehyde with $[IrH_3(PPh_3)_3]$ complex. This complex promoted the reduction using molecular hydrogen in refluxing acetic acid to afford the saturated alcohol in good (Scheme 4.3).[9]



Scheme 4.3 Hydrogenation of crotonaldehyde with $[IrH_3(PPh_3)_3]$ in acetic acid

Although significant effort has been made in the area of TH of unsaturated aldehydes with metal catalysts, there are still some challenges.[10] In recent years, a number of examples were published using alcohols such as ethanol or propanol as a hydrogen donor using catalysts based on platinum, iridium, ruthenium, rhodium, iron and cobalt for the TH of α,β-unsaturated aldehydes.[11] Generally, these reactions were performed either under reflux or under mild reaction conditions with a prolonged reaction time to give the saturated aldehyde or the fully reduced product as shown in Scheme 4.4.[9,12]



Scheme 4.4 Reduction of α,β-unsaturated aldehydes

With the shorter, linear alcohol methanol, it was reported that under these optimum catalytic conditions, the activity was severely redcued. These poor results are in agreement with the fact that methanol is more facial to form the acetal as a co-product alongside the desired alcohol, or the resulting formaldehyde from methanol dehydrogenation undergoes decarbonylation and deactivates the catalyst.[13–15] It should be noted that methanol was described to be inert in many catalytic systems, and this is because the dehydrogenation of methanol is less favourable thermodynamically at room temperature (ΔH^{o} = +91 KJ/mol). Therefore, to make the dehydrogenation feasible the presence of a good hydrogen acceptor could make TH with methanol thermodynamically a downhill reaction.[16]

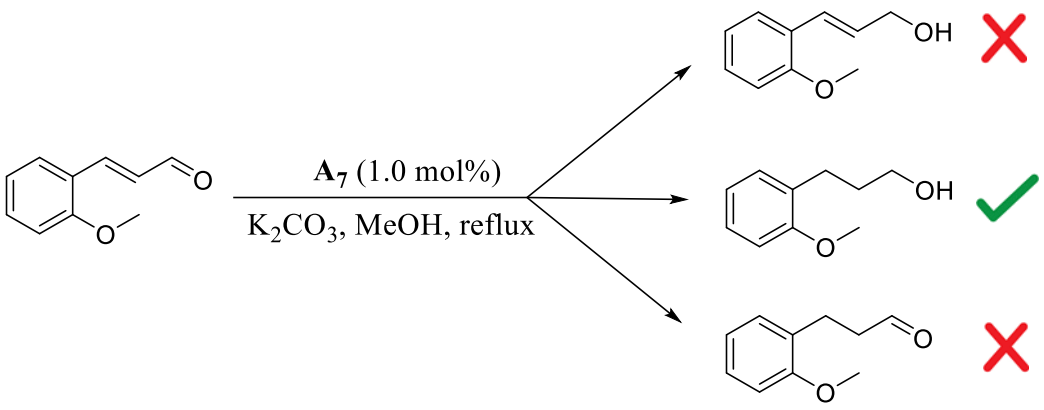
Lately, there is growing interest in the use of "green" chemistry for TH reactions, which includes the use of cheaper and safer sources of hydrogen and solvents, shorter reaction time with fewer steps of transformation, and more importantly the use of mild and aerobic reaction conditions. In this Chapter, our aim is to extend the application of the new rhodium catalyst **A**$_7$ to TH of α,β-unsaturated aldehydes using cheap methanol as both the source of hydrogen and reaction solvent.

4.2 Results and discussion

4.2.1 Optimisation of reaction conditions

Due to the relative importance of the hydrogenation products of α,β-unsaturated aldehydes, and the remarkable chemoselectivity of the rhodium complex **A**$_7$ presented in Chapters 2 and 3, the scope of our work was extended by examining the feasibility of the reduction of α,β-unsaturated aldehydes under the same conditions as in Chapter 3 with the current reduction system. 2-Methoxycinnamaldehyde was chosen as a model substrate for the reduction of unsaturated aldehydes. Surprisingly, under these reaction conditions, although **A**$_7$ was unable to reduce the unsaturated aldehydes chemoselectively, it catalysed the reduction of both the

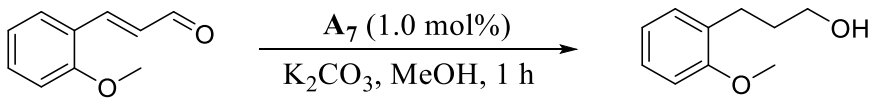
C=C and C=O double bonds to give only the saturated alcohol product, as shown in Scheme 4.5.



Scheme 4.5: Reduction of α,β-unsaturated aldehydes using **A**$_7$ with methanol

After that, an optimizing study was conducted, putting temperature as the target, expecting that varying the temperature would affect the speed of the rhodium hydride formation and delivery, which might enhance the possibility of reducing the unsaturated aldehyde selectively. Therefore, further experiments were conducted by lowering the temperature. The results of the optimization are shown in Table 4.1.

Table 4.1: Temperature optimization for the reduction of 2-methoxycinnamaldehyde with methanol



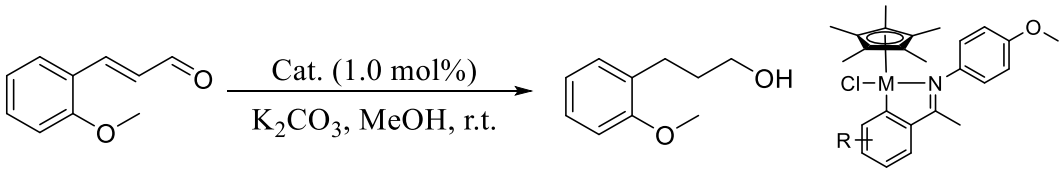
Entry[a]	Temperature ºC	Conversion %[b]
1	90	100
2	70	100
3	50	100
4	30	100
5	25	85

[a] Reaction conditions: aldehyde (0.3 mmol), catalyst (0.003 mmol), K_2CO_3 (0.075mmol) and MeOH (1.5 mL), stirred for 1h. [b] Conversion determined by ^{1}H-NMR spectroscopy.

Amazingly, lowering the temperature even to 25 ºC led to similar results and the same saturated alcohol was obtained as that at the higher temperature, in 85% conversion (Table 4.1, Entry 5). The full conversion was achieved by only raising the temperature to 30 ºC (Table 4.1, Entry 4). Judging from the activity, it is clear to say that complex **A7** is the first homogeneous catalyst that permits such transformation under such mild conditions. More importantly, the catalyst is capable to dehydrogenate methanol and transfer the hydrogen under ambient conditions.

Since such transformation is feasible with **A7** at room temperature, it was interesting to investigate if this reaction would be feasible without or with the use of different ligands. Therefore, we examined the dimeric $[Cp^*RhCl_2]_2$ and a wide range of cyclometalated complexes that were available and reported by our group for the TH of the model reaction. Table 4.2 shows the results of catalyst screening.

Table 4.2: Screening of catalyst for the TH of 2-methoxycinnamaldehyde with methanol



Entry[a]	Catalyst	M	R	Conversion %[b]
1	$[Cp^*RhCl_2]_2$	Rh	-	N.R
2	**A_1**	Rh	4-OCH_3	N.R
3	**A_2**	Rh	4,5-OCH_3	N.R
4	**A_3**	Rh	4,5$(CH)_4$	N.R
5	**A_4**	Rh	4-CN	N.R
6	**A_5**	Rh	4-NO_2	N.R
7	**A_6**	Rh	5-NO_2	N.R
8	**A_7**	Rh	4-OH	100
9	**A_8**	Rh	4-OH, 5-OCH_3	N.R
10	**A_9**	Ir	4-OCH_3	N.R
11	**A_{10}**	Ir	4,5-OCH_3	N.R
12	**A_{11}**	Ir	4,5$(CH)_4$	N.R
13	**A_{12}**	Ir	4-CN	N.R
14	**A_{13}**	Ir	4-NO_2	N.R
15	**A_{14}**	Ir	4-OH, 5-OCH_3	N.R
16*	**A_{15}**	Ir	4-OH	4

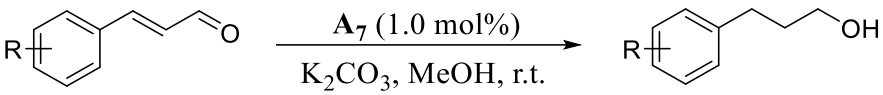
[a] Reaction conditions: aldehyde (0.3 mmol), catalyst (0.003 mmol), K_2CO_3 (0.075mmol) and MeOH (1.5 mL), stirred at 30 °C for 1h. [b] Conversion determined by ^{1}H-NMR spectroscopy.* The reaction was left for 4 h.

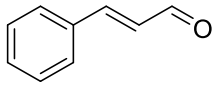
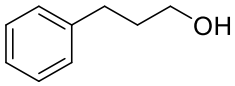
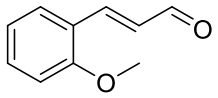
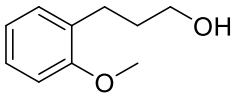
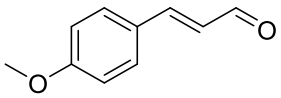
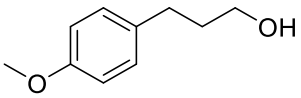
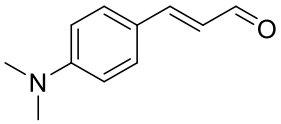
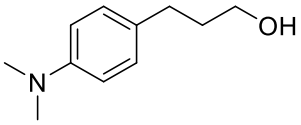
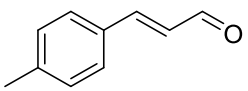
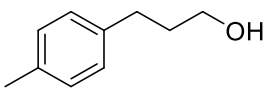
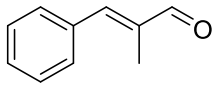
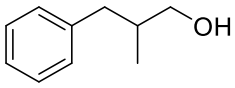
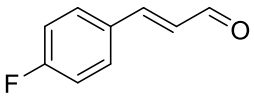
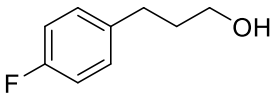
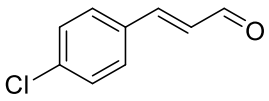
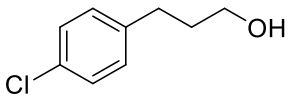
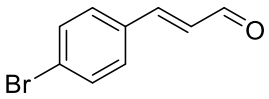
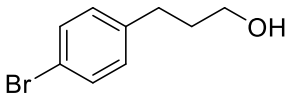
No reaction was observed when the dimeric $[Cp^*RhCl_2]_2$ was used for the reduction of 2-methoxycinnamaldehyde (Table 4.2, Entry 1). Also, all the other rhodium catalysts revealed no reaction (Table 4.2, Entries 2-8). Moreover, **A_8** which was observed to be active towards the selective reduction of aldehyde, (Chapter 2) showed no activity for the reduction of unsaturated aldehydes under the applied conditions (Table 4.2, Entry 9). Similarly, all the analogous iridium complexes that were reported to be highly efficient for the TH of various functional groups[17] were also generally inactive. It is noteworthy that catalyst **A_{15}**, which bears the -OH group, delivered only 4% conversion even after a prolonged time (Table 4.2, Entry 16). For the rest of the catalysts, the same phenomena were observed as those for rhodium complexes, which means no reaction was detected under the same reaction condition (Table 4.2, Entries 10-15). We finally examined the effect of different solvent, and it was shown that there was no reaction when the same experiment was performed using *i*PrOH.

4.2.2 Transfer hydrogenation of α,β-unsaturated aldehydes

By establishing the optimal conditions for the TH of unsaturated aldehydes, which were 1.0 mol% of **A_7** and 0.25 equiv. of K_2CO_3 at 30 ºC for 1 h, and to showcase the broader utility of the catalyst, this reaction system was successfully extended to a range of unsaturated aldehydes. The reaction was carried out with no need for an inert gas in an open vessel, and results of the reduction are summarised in Table 4.3.

Table 4.3: Substrate scope for the reduction of unsaturated aldehydes with methanol



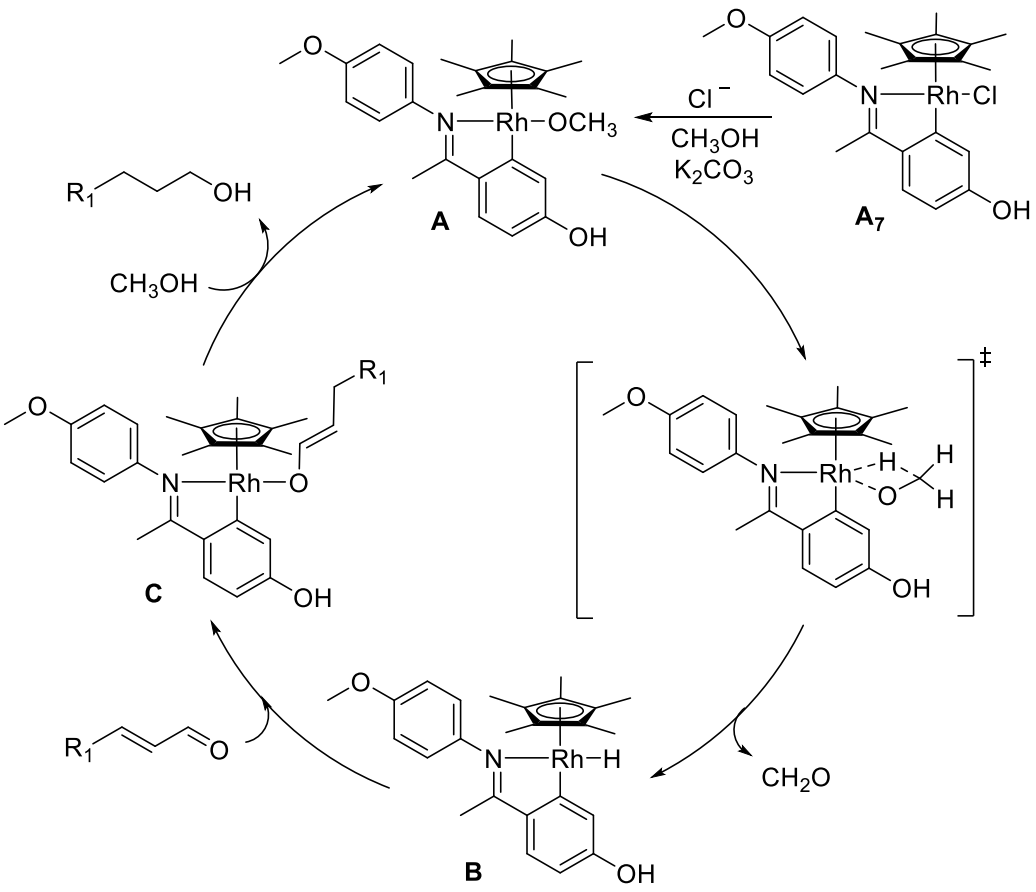
Entry[a]	Substrate	Product	Yield %[b]
1			89
2			93
3			85
4			79
5			74
6			83
7			91
8			69
9			74

Reaction conditions: aldehyde (0.3 mmol), catalyst (0.003 mmol), K_2CO_3 (0.075mmol) and MeOH (1.5 mL), stirred at 30 ºC for 1 h. [b] Yield determined by isolated product.

From the primary results shown in Table 4.3, **A_7** was found to be efficient under mild conditions, displaying a superb performance with good to excellent yields in the unsaturated aldehyde reduction. Thus, unsubstituted cinnamaldehyde and substituted cinnamaldehydes with electron-donating groups in *ortho* or *para* position were all effectively reduced in good to excellent yields (Entries 1-5). Similarly, substituted cinnamaldehydes with electron-withdrawing groups were also tolerated under the same condition to give the saturated products in moderate to excellent yields (Table 4.3, Entries 7-9). More importantly, substituents on α carbon such as $–CH_3$ led to a fully reduced product in good yields (Table 4.3, Entry 6).

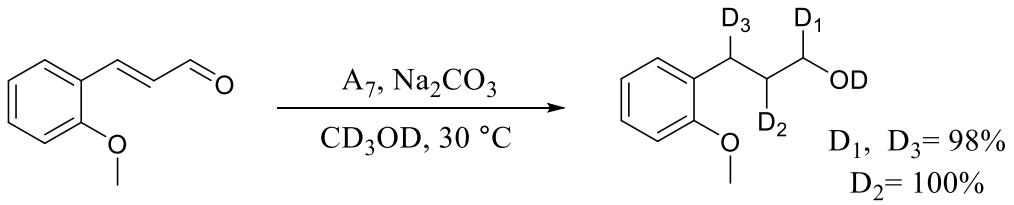
4.2.3 Mechanistic considerations

Scheme 4.6 illustrates the predicted catalytic cycle for the reduction of aldehyde with methanol on the basis of mechanisms that were proposed in Chapters 2 and 3. Methanol reacts with the dissociated form of catalyst **A_7** to produce complex **A**. Complex **A** is converted by hydrogen migration via the transition state shown to give the active rhodium species **B** and release formaldehyde. Next, the hydride migrates from species **B** to the unsaturated aldehyde affording the alkoxide complex **C**. In the next step, methanol protonates complex **C** to give the initial complex **A** and release the saturated alcohol product. As in the case of TH of α,β-unsaturated ketones, the hydroxyl group on the ligand may play a role in facilitating the hydride transfer from **B** via hydrogen bonding with the carbonyl oxygen.



Scheme 4.6: Proposed mechanism for the TH of unsaturated aldehydes

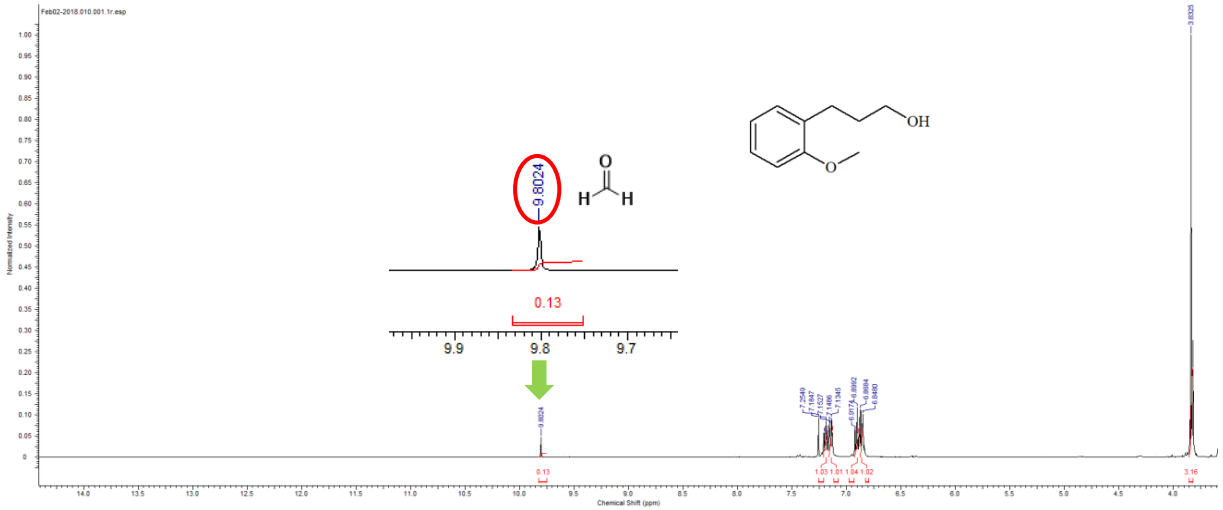
Duterated methanol was used for the reduction of 2-methoxycinnamaldehyde. The 1H-NMR confirmed the deuterium incorporation across the α,β-unsaturated system (See appendix) and thus verified that methanol is the only source of hydrogen during the TH (Scheme 4.7).



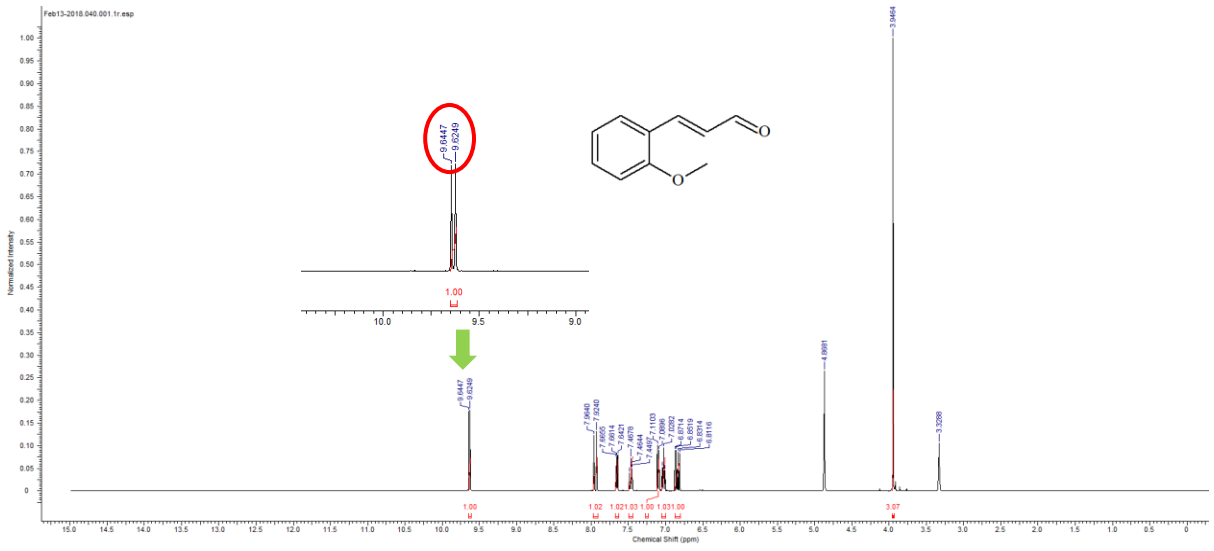
Scheme 4.9: TH of 2-methoxycinnamaldehyde with deuterated methanol

To gain more evidence, and to determine the fate of methanol and/or to confirm that methanol is dehydrogenated to formaldehyde, further experiments were conducted using the model reaction with the addition of a few drops of water in order to stabilise the formaldehyde. The

result of these studies, obtained with ^{1}H-NMR spectroscopy, indicates the presence of a new singlet peak that belongs to formaldehyde at around 9.80 ppm (Scheme 4.8). The substrate aldehyde shows a doublet and it is at 9.63 ppm as shown in Scheme 4.9. The formaldehyde chemical shift value is identical with that of pure formaldehyde as well as with what was reported in the literatures.[18]



Scheme 4.8: ^{1}H-NMR spectrum of formaldehyde in the presence of water



Scheme 4.9: ^{1}H-NMR spectrum of 2-methoxycinnamaldehyde in $CDCl_3$

4.3 Conclusion

This Chapter shows that the catalyst **A_7** exhibits high catalytic activity towards the TH of unsaturated aldehydes to the corresponding saturated alcohols at room temperature. The transformation proceeds through methanol dehydrogenation under mild conditions to produce formaldehyde as a co-product and hydrogen that is used for the hydrogenation of both carbonyl and olefin functionalities of α,β-unsaturated aldehydes. This transformation confirms that for the first time methanol can be easily dehydrogenated at room temperature with a homogeneous catalyst under mild conditions.

4.4 Experimental and analytical data

4.4.1 General information

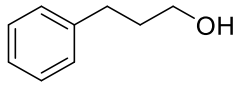
Unless otherwise specified, all reactions were carried out under an open atmosphere using standard techniques. All chemicals that were used in the synthesis of ligands and catalysts were purchased from commercial suppliers and used as they received i.e. without further purification, and methanol was HPLC grade. TLC silica gel 60F254 (Merck) plates were used for the analytical thin-layer chromatography and they were revealed under ultra-violet irradiation, potassium permanganate or iodine. All columns were run using a mixture of hexane/ethyl acetate and silica gel 60 Å (230-400 mesh). ^{1}H-NMR and ^{13}C-NMR spectra were recorded with a Bruker 400 MHz spectrometer using $CDCl_3$ as a solvent with tetramethylsilane (TMS) as the internal standard at 25 ºC. Processing and interpretation were performed with ACD- labs 12.0 (Advanced Chemistry Development Inc.). The multiplicity of the signals is abbreviated as bs (broad singlet), s (singlet), d (doublet), dd (doublets of doublet), ddd (doublet of doublet of doublet), td (triplets of doublet), p (pentet) or m (multiplet). High-resolution mass spectrum was taken by chemical ionisation (CI) at the Analytical Services of the Department

of Chemistry, University of Liverpool. ^{1}H-NMR, 1^{3}C-NMR and HRMS for all the products were collected, and the NMR data are consistent with the reported literature.

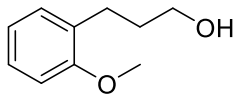
4.4.2 General procedure for the TH of unsaturated aldehydes in methanol

Aldehyde (0.3 mmol), catalyst (0.003 mmol) and K_2CO_3 (0.075mmol) were dissolved in MeOH (1.5 mL) in a Radleys tube. The reaction mixture was then stirred at 30 $^{\circ}$C for 1 h. After completion, the solvent was removed under vacuum. The resulting crude product was purified by flash chromatography using a mixture of hexane and ethyl acetate.

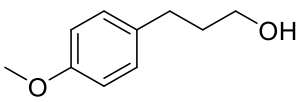
4.4.3 Analytical data of saturated alcohol products



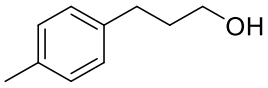
3-phenylpropan-1-ol:[19] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.32-7.16 (m, 5H), 3.67 (t, J = 6.3 Hz, 2H), 2.70 (t, J = 7.6 Hz, 2H), 1.94-1.84 (m, 2H), 1.47 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 141.94, 128.54, 128.52, 125.98, 62.39, 34.34, 32.20; HRMS for $C_9H_{12}O$ $[(M - H_2O) + H]^+$: m/z calc.: 119.0855; found: 119.0859.



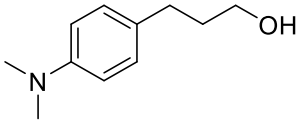
3-(2-Methoxyphenyl)propan-1-ol:[20] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.19 (t, J = 7.7 Hz, 1H), 7.14 (d, J = 7.4 Hz, 1H), 6.90 (t, J = 7.4 Hz, 1H), 6.86 (d, J = 8.2 Hz, 1H), 3.83 (s, 3H), 3.59 (t, J = 6.2 Hz, 2H), 2.72 (t, J = 7.3 Hz, 2H), 1.84 (p, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 157.40, 130.12, 129.97 127.20, 120.73, 110.32, 61.95, 55.73, 32.93, 25.91; HRMS for $C_{10}H_{14}O_2$ $[M + H]^+$: m/z calc.: 167.1067; Found: 167.1072.



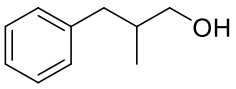
3-(4-Methoxyphenyl)propan-1-ol:[21] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.11 (d, J = 8.5 Hz, 2H), 6.83 (d, J = 8.5 Hz, 2H), 3.78 (s, 3H), 3.66 (t, J = 6.4 Hz, 2H), 2.64 (t, J = 7.5 Hz, 2H), 1.85 (p, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 157.81, 133.85, 129.30, 113.82, 62.26, 55.26, 34.43, 31.14; HRMS for $C_{10}H_{14}O_2$ $[M + NH_4]^+$: m/z calc184.1332; Found: 184.1339.



3-(P-tolyl)propan-1-ol:[22] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.09 (s, 4H), 3.66 (t, J = 6.5 Hz, 2H), 2.66 (t, J = 7.5 Hz, 2H), 2.31 (s, 3H), 1.90-1.83 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 138.70, 135.32, 129.09, 128.30, 62.34, 34.34, 31.63, 20.98; HRMS for $C_{10}H_{14}O$ $[M + NH_4]^+$: m/z calc.: 168.1383; Found: 168.1387.

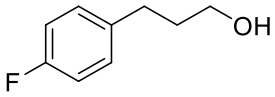


3-(4-(Dimethylamino)phenyl)propan-1-ol:[23] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.08 (d, J = 8.6 Hz, 2H), 6.70 (d, J = 8.6 Hz, 2H), 3.66 (t, J = 6.4 Hz, 2H), 2.90 (s, 6H), 2.61 (t, J = 7.4 Hz, 2H), 1.89-1.82 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 149.12, 129.92, 128.99, 113.09, 62.48, 40.92, 34.52, 31.02; HRMS for $C_{11}H_{17}NO$ $[M + H]^+$: m/z calc.: 180.1383; Found: 180.1391.

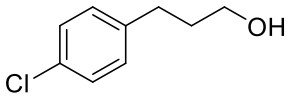


2-Methyl-3-phenylpropan-1-ol:[24] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.29-7.25 (m, 2H), 7.20-7.16 (m, 3H), 3.53 (dd, J = 10.5, 5.8 Hz, 1H), 3.47 (dd, J = 10.5, 6.0 Hz, 1H), 2.75

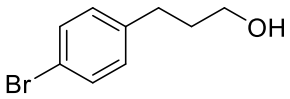
(dd, J = 13.4, 6.2 Hz, 1H), 2.42 (dd, J = 13.4, 8.0 Hz, 1H), 1.98-1.90 (m, 1H), 0.92 (d, J = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 140.62, 129.14, 128.27, 125.88, 67.68, 39.72, 37.80, 16.46; HRMS for $C_{10}H_{14}O$ $[M + NH_4]^+$: m/z calc.: 168.1383; Found: 168.1388.



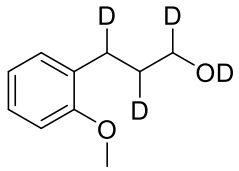
3-(4-Fluorophenyl)propan-1-ol:[25] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.14 (dd, J = 8.5, 5.5 Hz, 2H), 7.00-6.93 (m, 2H), 3.65 (t, J = 6.4 Hz, 2H), 2.67 (t, J = 7.1 Hz, 2H), 1.89-1.82 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 161.27 (d, J_{C-F} = 243.52 Hz), 137.39 (d, J_{C-F} = 3.06 Hz), 129.73 (d, J_{C-F} = 7.66 Hz) , 115.10 (d, J_{C-F} = 20.68 Hz), 62.04, 34.28, 31.21; HRMS for $C_9H_{11}FO$ $[M + NH_4]^+$: m/z calc.: 172.0876; Found: 172.0873.



3-(4-Chlorophenyl)propan-1-ol:[22] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.25 (d, J = 8.6 Hz, 2H), 7.12 (d, J = 8.3 Hz, 2H), 3.66 (t, J = 6.3 Hz, 2H), 2.68 (t, J = 7.5 Hz, 2H), 1.89-1.82 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 140.23, 131.58, 129.77, 128.48, 127.65, 62.01, 34.06, 31.38; HRMS for $C_9H_{11}ClO$ $[M + NH_4]^+$: m/z calc.: 188.0513; Found: 188.0496.



3-(4-Bromophenyl)propan-1-ol:[20] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.40 (d, J = 8.2 Hz, 2H), 7.07 (d, J = 8.3 Hz, 2H), 3.66 (t, J = 6.4 Hz, 2H), 2.66 (t, J = 7.4 Hz, 2H), 1.89-1.82 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 140.76, 131.43, 130.20, 119.58, 62.00, 34.01, 31.45; HRMS for $C_9H_{11}FO$ $[M + NH_4]^+$: m/z calc.: 232.0332; Found: 232.0332.



3-(2-Methoxyphenyl)propan-1,2,3-d3-1-ol-d: ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.18 (t, J = 7.6 Hz, 1H), 7.15 (d, J = 7.4 Hz, 1H), 6.90 (t, J = 7.4 Hz, 1H), 6.86 (d, J = 8.2 Hz, 1H), 3.83 (s, 3H), 3.56 (s, 1H), 2.72 (s, 1H), 1.76 (s, 1H).

4.5 References

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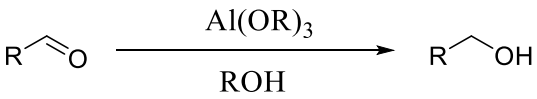
Chapter 5

Chemoselective transfer hydrogenation of mono- and di-aldehydes

5.1 Introduction

The reduction of mono- and di-aldehydes into the corresponding primary alcohols and hydroxymethyl aldehydes compounds is one of the fundamental functional group transformations. The importance of these compounds come from their usage as a valuable precursor in agrochemicals, medicals and fine chemical industry.[1–3] As reported previously, TH of aldehydes is one of the difficult processes because aldehyde may undergoe decarbonylation and poison the catalyst by moving the carbonyl from aldehyde to the metal, or deprotonation of the CH group which is α to the carbonyl under basic condition to form the aldol or related products.[4] The first example for the TH of aldehydes was discovered in 1925 independently by Verely, Meerwein and Schmidt using aluminium ethoxide in ethanol, as shown in the following equation.[5,6]



In recent years, many attempts have been made in the area of carbonyl reductions to enable fast, selective and productive TH. Different catalytic systems were developed based on varied metals, such as Ru, Rh, Ir, Fe, Au, Co and Ag.[7–13] The significant advance in TH of carbonyl compounds was made by Noyori and co-workers when they demonstrated the ruthenium complexes (Ru-TsDPEN) for the asymmetric reduction of various ketones.[14] Such discovery has inspired many researchers to develop a variety of related metal catalysts that are capable of the TH of carbonyl compounds. Examples include the rhodium N-heterocyclic carbene complexes introduced by Crabtree and co-workers for the asymmetric TH of C=O and C=N bonds,[4] and the iridium monotosylated ethylenediamine reported by Wu of our group for efficient TH of various aliphatic and aromatic aldehydes under aqueous conditions.[15] Whilst many catalysts were described with high selectivity for the reduction of aldehydes, the selective

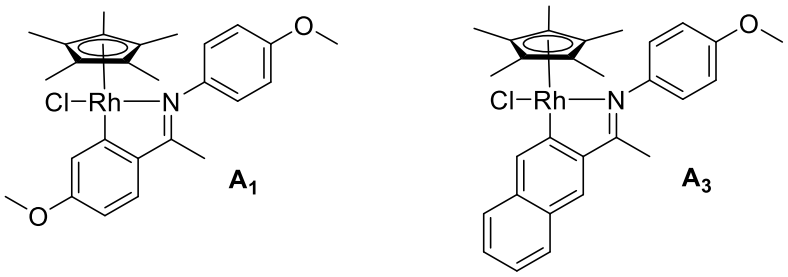
reduction of di-aldehydes is still challenging and remain little unexplored by TH. Only a few examples have been reported in the selective reduction of di-aldehyde area. For example, Sello *et al*. investigated an enzymatic catalyst for the reduction of di-aldehydes using E. coli JM109 with about 25% conversion.[16] Verma and co-worker demonstrated that nickel phthalocyanine can regioselectively hydrogenate 1,3- and 1,4-dialdehydes to the corresponding alcohols. However, the drawback of this system is the reduction of both aldehyde groups in case of 1,2-dialdehyde.[17]

Given the importance of the chemoselective reduction of di-aldehydes, this chapter presents for the first time that our rhodium complexes are indeed capable of selectively hydrogenating functionalized aromatic and heteroaromatic aldehydes into alcohols, using formic acid as the hydrogen source under mild reaction conditions.

5.2 Results and discussion

5.2.1 Optimisation of reaction conditions

Based on the previous work of our group[18] where iridium complexes were employed as a catalyst for the TH of aldehydes with formic acid, we chose to determine the catalytic potential of rhodium complexes for such reactions.

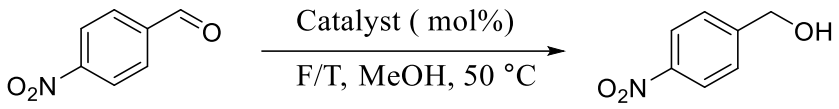


Scheme 5.1: Rhodium complexes **A₁** and **A₃**

Initial experiments for the reduction of 4-nitrobenzaldehyde with formic acid was conducted using 0.01 mol% of **A₁** and **A₃** complexes as a stock MeOH solution. All the reactions were

tested by TLC after 30 minutes and then left for longer time (1 h). However, all results were disappointing especially when using complex **A3**. However, doubling the catalyst loading revealed that **A1** resulted in a better conversion, and it is shown that 0.2 mol% of complex **A1** was sufficient for the reduction to complete within 30 minutes under an ambient condition. Further optimization of reaction temperature showed that 50 ºC is the optimum for the reaction to complete under the applied reaction conditions. Results of catalyst and temperature screening for the reduction of 4-nitrobenzaldehyde were summarised in Table 5.1.

Table 5.1: Screening of catalysts and temperature for the TH of 4-nitrobenzaldehyde



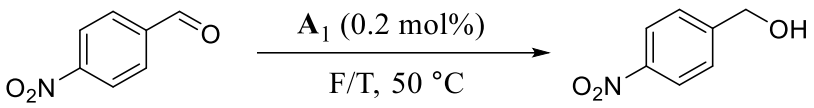
Entry[a]	Catalyst	Cat.(mol%)	Temperature ºC	Conversion %[b]
1	$[Cp^*RhCl_2]_2$	0.2	50	12
2	**A1**	0.2	50	100
3	**A3**	0.2	50	60
4	**A1**	0.1	50	89
5*	**A1**	0.2	40	90

[a] Reaction conditions: aldehyde (0.5 mmol), catalyst, F/T = HCO_2H/Et_3N (5:2) azeotrope (0.5 mL), solvent (0.5 mL), stirred at 50 ºC for 30 min. [b] Conversion determined by ^{1}H-NMR spectroscopy. * The reaction was left for 60 min.

Results from Table 5.1 show that the presence of the imine ligand (complex **A1**) increases the conversion from 12% for the dimeric $[Cp^*RhCl_2]_2$ (Table 5.1, Entry 1) to 100% (Table 5.1, Entry 2) in 30 minutes. Furthermore, lowering the temperature results in lower conversion even when the reaction was left for a longer period of time (Table 5.1, Entry 5).

Following the optimization of catalyst and temperature, to further improve the conversion we switched to investigating the influence of different solvents on the reduction. Results of solvent screening are shown in Table 5.2.

Table 5.2: Screening of solvent for the reduction of 4-nitro benzaldehyde



Entry[a]	Solvent	Conversion %[b]
1	MeOH	100
2	-	90
3	DCM	70
4	H_2O	20
5	TFE	6

[a] Reaction conditions: aldehyde (0.5 mmol), catalyst **A_1** (0.001 mmol), HCO_2H/Et_3N (5:2) azeotrope (0.5 mL) and solvent (0.5 mL), stirred at 50 ºC for 30 min. [b] Conversion determined by ^{1}H-NMR spectroscopy.

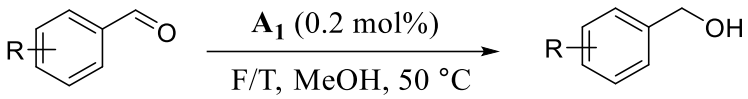
Results from Table 5.2 demonstrate that methanol was the best solvent for the reduction (Table 5.2, Entry 1), and this is consistent with the results presented in previous chapters. Interestingly, when the reaction was conducted under solvent-free conditions, excellent conversion of 90% was also obtained (Table 5.2, Entry 2). However, other solvents were shown to be less efficient, resulting in significantly sluggish reduction of the aldehyde (Table 5.2, Entries 3-5).

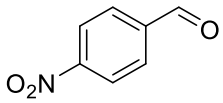
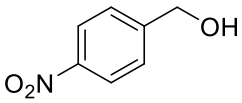
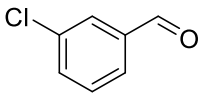
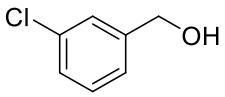
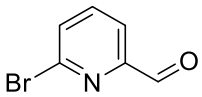
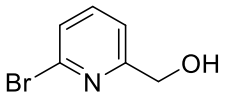
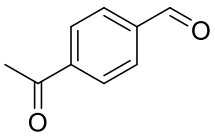
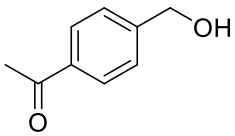
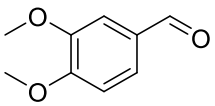
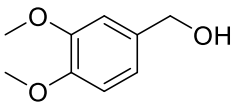
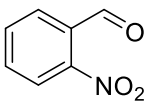
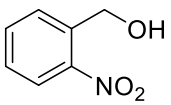
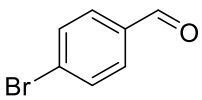
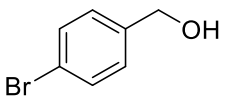
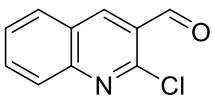
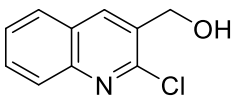
5.2.2 Transfer hydrogenation of mono-aldehydes with formic acid

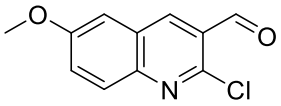
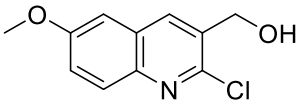
Once the optimal reduction conditions were established, and to evaluate the catalytic performance, it became interesting to expand the substrate scope for the reduction of diversely

substituted aldehydes. Table 5.3 illustrates the results for the substrate scope of TH of aldehydes.

Table 5.3: TH of mono-aldehydes with formic acid



Entry[a]	Substrate	Product	Yield %[b]
1			92
2			88
3			96
4			95
5			86
6			91
7			93
8			87

9			89

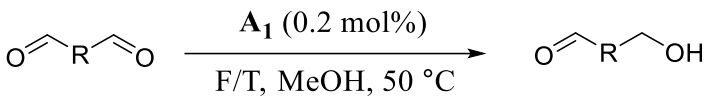
[a] Reaction conditions: aldehyde (0.5 mmol), catalyst **A_1** (0.001 mmol), HCO_2H/Et_3N (5:2) azeotrope (0.5 mL) and MeOH (0.5 mL), stirred at 50 ºC for 30 min. [b] Yield determined by isolated product.

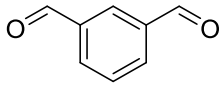
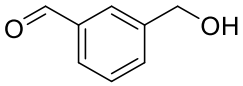
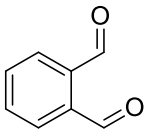
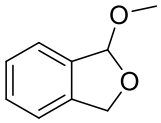
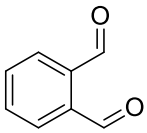
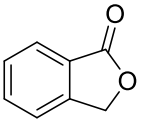
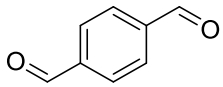
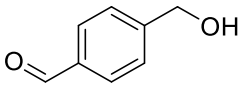
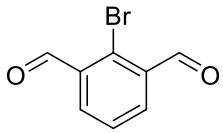
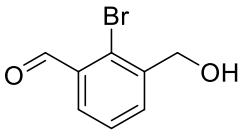
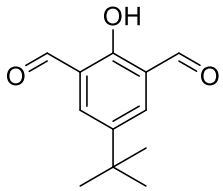
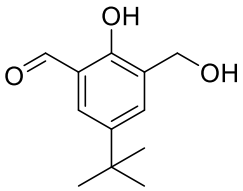
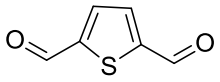
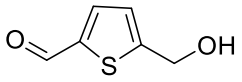
The aldehydes substrate scope show that complex **A_1** is active towards the aldehydes that were tested. All aldehydes reacted easily regardless of the nature of substituents and their positions to give the corresponding alcohols in good to excellent isolated yields (86-96%). Sensitive electron-withdrawing groups, such as nitro and halo in different positions, did not reduce the catalyst activity (Table 5.3, Entries 1, 2, 6 and 7). Also, electron-donating functional groups, such as methoxy ($-OCH_3$), exhibit an insignificant effect on the yield (Table 5.3, Entry 5). Moreover, heterocycles and other functional groups such as ketones were also left intact under the applied reaction condition (Table 5.3, Entries 3, 4, 8 and 9).

5.2.3 Transfer hydrogenation of di-aldehydes with formic acid

Based on the high selectivity and reactivity of complex **A_1** for the TH of mono-aldehydes, we were interested in extending the reduction system to a more challenging reduction, which is the selective reduction of di-aldehyde compounds. Table 5.4 shows the outcome of the reduction of di-aldehyde with complex **A_1**.

Table 5.4: TH of di-aldehydes with formic acid



Entry[a]	Substrate	Product	Yield %[b]
1			94
2[c]			65
3[d]			50
4			70
5			64
6			70
7			72

[a] Reaction conditions: aldehyde (0.5 mmol), catalyst **A1** (0.001 mmol), HCO_2H/Et_3N (5:2) azeotrope (0.5 mL) and MeOH (0.5 mL), stirred at 50 ºC for 30 min. [b] Yield determined by isolated product. [c] 80 ºC. [d] 25 ºC.

Contrary to our expectation that under the reaction conditions the catalyst would promote the reduction of both aldehyde groups, results from Table 5.4 demonstrate that the catalyst promotes the reduction of only one aldehyde group leaving the second group intact. Unsubstituted di-aldehydes were all viable, furnishing good to excellent yields under the applied conditions (Table 5.4, Entries 1 and 4). Furthermore, for the 1,2-di-aldehyde substrate (Table 5.4, Entries 2 and 3), two different cyclic products were obtained by varying the temperature. Presumably, the room temperature, kinetic product is converted to the thermodynamic product via acid and rhodium catalysis as illustrated in Figure 1. Moreover, the sterically bulky substituents were also tolerated in the selective reduction of di-aldehydes and resulted in good yields (Table 5.4, Entries 5, 6 and 7).

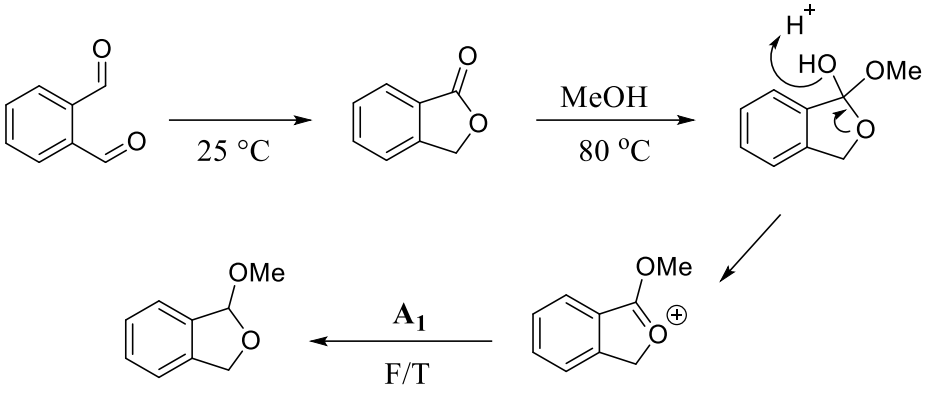


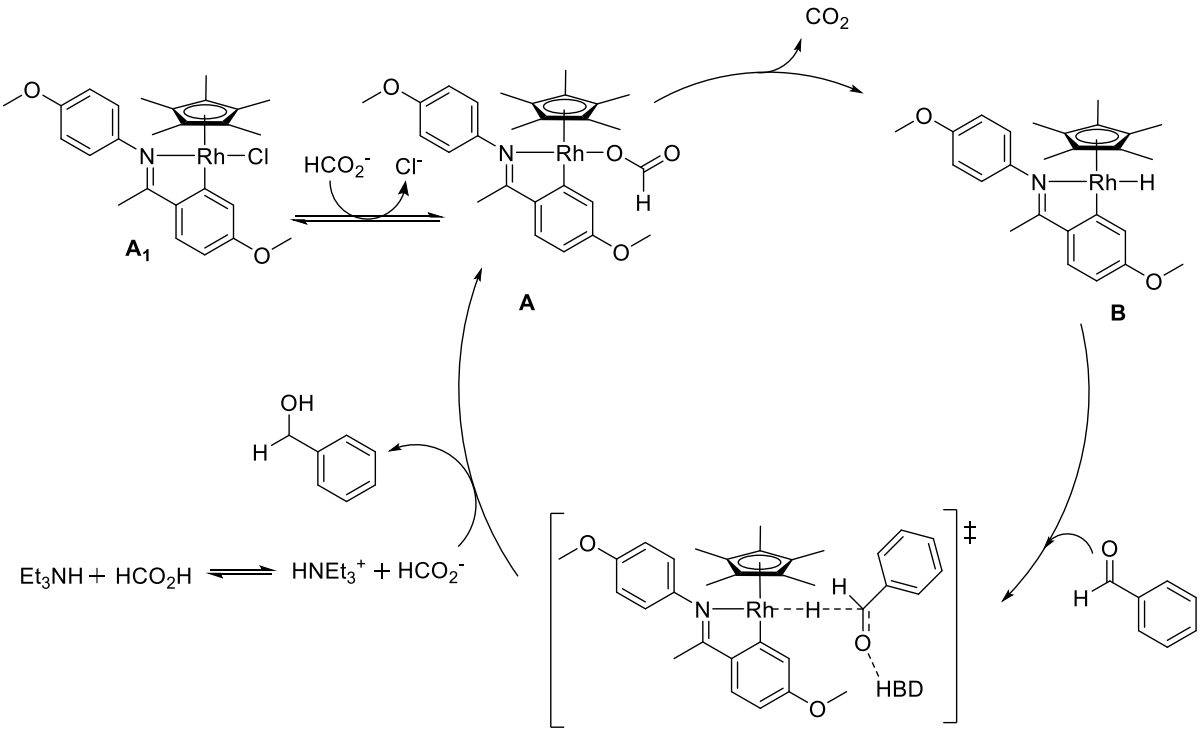
Figure 1: Products obtained from the TH of 1,2-dialdehyde

To the best of our knowledge, complex **A1** is the first example that provides a high chemoselectivity towards the reductions of di-aldehydes to their corresponding hydroxymethyl aldehydes.

5.2.4 Mechanistic considerations

A possible mechanism for the TH of aldehydes is shown in Scheme 5.2. This plausible mechanism is proposed on the basis of the previous study of our group for the iridacycle-catalysed TH with formic acid and related literature.[19,20] The first step involves the formation

of complex **A** as a result of the presence of formic acid and/or formate. Then complex **A** undergoes decarboxylation of the formate releasing CO_2 and leading to the formation of active rhodium hydride species **B**. In the next step, the hydride is transferred from complex **B** to the carbonyl carbon of the aldehyde, while the aldehyde is activated via hydrogen bonding as shown in the transition state.[21] Then with the aid of formic acid, the resulting alcohol product is formed and complex **A** is regenerated for the next cycle.



Scheme 5.2: Proposed catalytic cycle for the TH of aldehydes (HBD: hydrogen bond donor, which could be formic acid or triethylamonium cation)

5.3 Conclusion

This Chapter demonstrates a new protocol of rhodium complex that affords highly chemoselective TH, especially for challenging di-aldehyde compounds using formic acid as a source of hydrogen. This transformation proceeds under mild conditions, necessitating no inert atmosphere and special equipment. It also provides an easy and efficient synthesis of primary alcohols and hydroxymethyl carbonyl compounds which are important for the production of pharmaceuticals, fine chemicals and agrochemicals.

5.4 Experimental and analytical data

5.4.1 General information

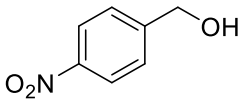
Unless otherwise specified, all reactions were carried out under aerobic atmosphere using standard techniques. All chemicals that were used in the reactions including the F/T mixture were purchased from commercial suppliers and used without further purification, and methanol was HPLC grade. TLC silica gel 60F254 (Merck) plates were used for the analytical thin-layer chromatography and they were revealed under ultra-violet irradiation, potassium permanganate or iodine. All columns were run using a mixture of hexane/ethyl acetate and silica gel 60 Å (230-400 mesh). ^{1}H-NMR and ^{13}C-NMR spectra were recorded with a Bruker Avance 400 MHz spectrometer using $CDCl_3$ as a solvent with tetramethylsilane (TMS) as the internal standard at 25 ºC. Processing and interpretation were performed with ACD-labs 12.0 (Advanced Chemistry Development Inc.). The multiplicity of the signals is abbreviated as bs (broad singlet), s (singlet), d (doublet), dd (doublets of doublet), ddd (doublet of doublet of doublet), td (triplets of doublet), or m (multiplet). High-resolution mass spectrum was taken by chemical ionisation (CI) at the Analytical Services of the Department of Chemistry, University of Liverpool. ^{1}H-NMR, ^{13}C-NMR and HRMS for all the products were collected, and the NMR data are consistent with the reported literature.

5.4.2 General procedure for the TH of aldehydes

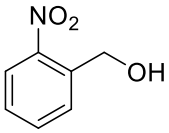
Aldehyde (0.5 mmol) and a stock solution of catalyst **A₁** ($1x10^{-3}$ mmol) in (0.1 mL) MeOH were placed in a Radlys tube, followed by adding MeOH (0.4 mL) and formic acid/trimethylamine azeotrope (0.5 mL). The reaction mixture was stirred at 50 ºC for 30 min. At the end of the reaction, the resulting mixture was quenched with aqueous $NaHCO_3$ solution and extracted with ethyl acetate, dried over $MgSO_4$ and purified by flash chromatography

(hexane/ethyl acetate). For di-aldehydes, the resulting mixture was extracted without quenching.

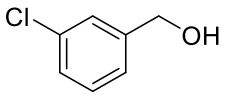
5.4.3 Analytical data of alcohol products



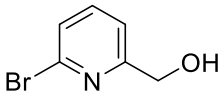
4-Nitrophenyl methanol:[22] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 8.23 (d, J = 8.4 Hz, 2H), 7.54 (d, J = 8.4 Hz, 2H), 4.84 (d, J = 5.4 Hz, 2H), 1.90 (t, J = 5.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 148.08, 127.00, 123.76, 64.05; HRMS for $C_7H_7NO_3$ $[M + H]^+$: m/z calc.: 154.0499; found: 154.0503.



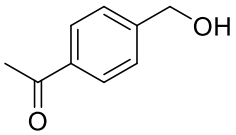
2-Nitrophenyl methanol:[23] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 8.11 (d, J = 8.2 Hz, 1H), 7.75 (d, J = 7.6 Hz, 1H), 7.68 (t, J = 7.4 Hz, 1H), 4.48 (t, J = 7.6 Hz, 2H), 4.98 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 147.69, 136.76, 134.14, 130.03, 128.53, 125.04, 62.06; HRMS for $C_7H_7NO_3$ $[(M – H_2O) + H]^+$: m/z calc.: 136.0393; found: 136.0396.



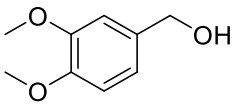
3-Chlorophenyl methanol:[24] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.35 (s, 1H), 7.30-7.21 (m, 3H), 4.67 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 142.83, 134.45, 129.82, 127.71, 126.96, 124.84, 64.55; HRMS for C_7H_7ClO $[(M – H_2O) + H]^+$: m/z calc.: 125.0153; found: 125.0155.



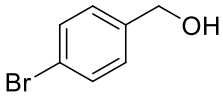
6-Bromopyridin-2-methanol:[25] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.56 (t, J = 7.8 Hz, 2H), 7.40 (d, J = 7.8 Hz, 1H), 7.29 (d, J = 7.5 Hz, 1H), 4.75 (d, J = 5.3 Hz, 2H), 3.15 (t, J = 4.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 161.17, 141.41, 139.09, 126.68, 119.30, 64.19; HRMS for C_6H_6BrNO $[M + H]^+$: m/z calc.: 187.9706; found: 187.9706.



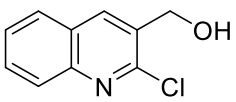
4-Acetyl phenylmethanol:[26] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.92 (d, J = 8.2 Hz, 2H), 7.44 (d, J = 8.2 Hz, 2H), 4.76 (s, 2H), 2.58 (s, 3H), 2.42 (bs, 1H) ; ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 198.04, 146.29, 136.29, 128.63, 126.62, 64.57, 26.66; HRMS for $C_9H_{10}O_2$ $[M + H]^+$: m/z calc.: 151.0754; found: 151.075.



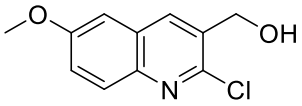
3,4-Dimethoxyphenyl)methanol:[23] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 6.92 (s 1H), 6.90 (d, J = 8.2 Hz, 1H), 6.84 (d, J = 8.1 Hz, 1H), 4.62 (s, 2H), 3.89 (s, 3H), 3.87 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 149.13, 148.61, 133.58, 119.41, 111.08, 110.48, 65.33, 55.96, 55.85; HRMS for $C_9H_{12}O_3$ $[M + H]^+$: m/z calc.: 169.0764; found: 169.0763.



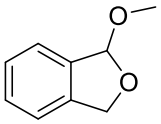
4-Bromophenyl methanol:[22] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.48 (d, J = 8.3 Hz, 1H), 7.23 (d, J = 8.3 Hz, 2H), 4.64 (s, 2H), 1.82 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 139.89, 131.76, 128.72, 121.59, 64.72; HRMS for C_7H_7BrO $[M]^+$: m/z calc.: 185.9913; found: 185.9922.



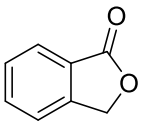
2-Chloroquinolin-3-methanol:[27] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 8.29 (s, 1H), 8.02 (d, J = 8.4 Hz, 1H), 7.85 (d, J = 8.1 Hz, 1H), 7.72 (t, J = 7.2 Hz, 1H), 7.57 (t, J = 7.3 Hz, 1H), 4.94 (d, J = 5.5 Hz, 2H), 2.24 (t, J = 5.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 149.07, 146.97, 136.24, 132.32, 130.25, 128.25, 127.56, 127.37, 127.22, 62.05; HRMS for $C_{10}H_8ClNO$ $[M + H]^+$: m/z calc.: 194.0354; found: 194.0353.



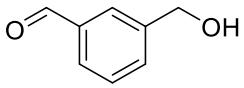
2-Chloro-6-methoxyquinolin-3-methanol:[28] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 8.18 (s, 1H), 7.91 (d, J = 9.2 Hz, 1H), 7.37 (dd, J = 9.2, 2.6 Hz, 1H), 7.10 (d, J = 2.5 Hz, 1H), 4.91 (d, J = 5.6 Hz, 2H), 3.93 (s, 3H), 2.17 (t, J = 5.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 158.28, 142.92, 135.08, 132.46, 129.62, 128.49, 122.79, 105.20, 62.11, 55.61; HRMS for $C_{11}H_{10}ClNO_2$ $[M + H]^+$: m/z calc.: 224.0473; found: 224.0471.



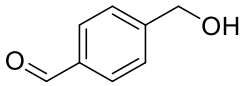
1-Methoxy-1,3-dihydroisobenzofuran:[29] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.40 (d, J = 8.0 Hz, 1H), 7.35 (t, J = 8.0 Hz, 2H), 7.27 (d, J = 8.0 Hz, 1H), 6.18 (s, 1H), 5.22 (d, J = 12.6 Hz, 1H), 5.05 (d, J = 12.6 Hz, 1H), 3.43 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 139.95, 137.31, 129.21, 127.68, 122.97, 121.03, 107.60, 72.36, 54.26; HRMS for $C_9H_{10}O_2$ $[M + H]^+$: m/z calc.: 151.0759; found: 151.0765.



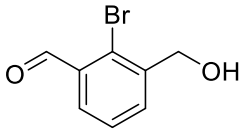
Isobenzofuran-1(3H)-one:[30] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 7.94 (d, J = 8.0 Hz, 1H), 7.69 (t, J = 7.6 Hz, 1H), 7.56 (d, J = 7.6 Hz, 1H), 7.51 (d, J = 7.6 Hz, 1H), 5.33(s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 171.09, 146.53, 134.01, 129.05, 125.80, 125.77, 122.09, 69.64; HRMS for $C_8H_6O_2$ $[M + H]^+$: m/z calc.: 135.0441; found: 135.0439.



3-Hydroxymethyl benzaldehyde:[31] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 10.03 (s, 1H), 7.89 (s, 1H), 7.81 (d, J = 7.6 Hz, 1H), 7.65 (d, J = 7.5 Hz, 1H), 7.53 (t, J = 7.5 Hz, 1H), 4.80 (s, 2H), 1.90 (bs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 192.27, 141.96, 136.65, 132.80, 129.24, 129.03, 127.80, 64.51; HRMS for $C_8H_8O_2$ $[M + H]^+$: m/z calc.: 137.0749; found: 137.0754.

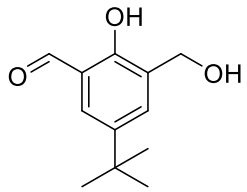


4-Hydroxymethyl benzaldehyde:[31] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 9.98 (s, 1H), 7.85 (d, J = 7.9 Hz, 2H), 7.52 (d, J = 7.9 Hz, 2H), 4.79 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 192.06, 147.80, 135.68, 130.03, 126.97, 64.56; HRMS for $C_8H_8O_2$ $[M + NH_4]^+$: m/z calc.: 154.0863; found: 154.0869.

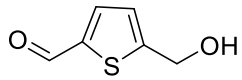


2-Bromo-3-hydroxymethyl benzaldehyde:[32] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 10.45 (s, 1H), 7.85 (d, J = 7.6 Hz, 1H), 7.78 (d, J = 7.5 Hz, 1H), 7.46 (t, J = 7.5 Hz, 1H), 4.85

(s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 191.98, 141.31, 133.99, 129.03, 127.86, 126.20, 64.47; HRMS for $C_8H_7BrO_2$ [(M – H_2O)+ H]$^+$: m/z calc.: 198.9753; found: 198.9756.



2-Hydroxy-3-hydroxymethyl-5-tert-butylbenzaldehyde:[33] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 11.20 (s, 1H), 9.90 (s, 1H), 7.63 (s, 1H), 7.47 (s, 1H), 4.76 (s, 2H), 1.33 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 195.96, 157.38, 142.79, 133.67, 129.07, 128.75, 119.83, 61.01, 34.17, 31.25; HRMS for $C_{12}H_{16}O_3$ [M + Na]$^+$: m/z calc.: 231.1009; found:231.0997.



5-Hydroxymethyl thiophene-2-carbaldehyde:[34] ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) δ (ppm): 9.86 (s, 1H), 7.67 (d, J = 3.6 Hz, 1H), 7.11 (d, J = 3.6 Hz, 1H), 4.90 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, 298 K) δ (ppm): 182.96, 155.17, 143.09, 136.57, 125.54, 60.41; HRMS for $C_6H_6O_2S$ [M + H]$^+$: m/z calc.: 143.0161; found: 143.0158.

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Chapter 6

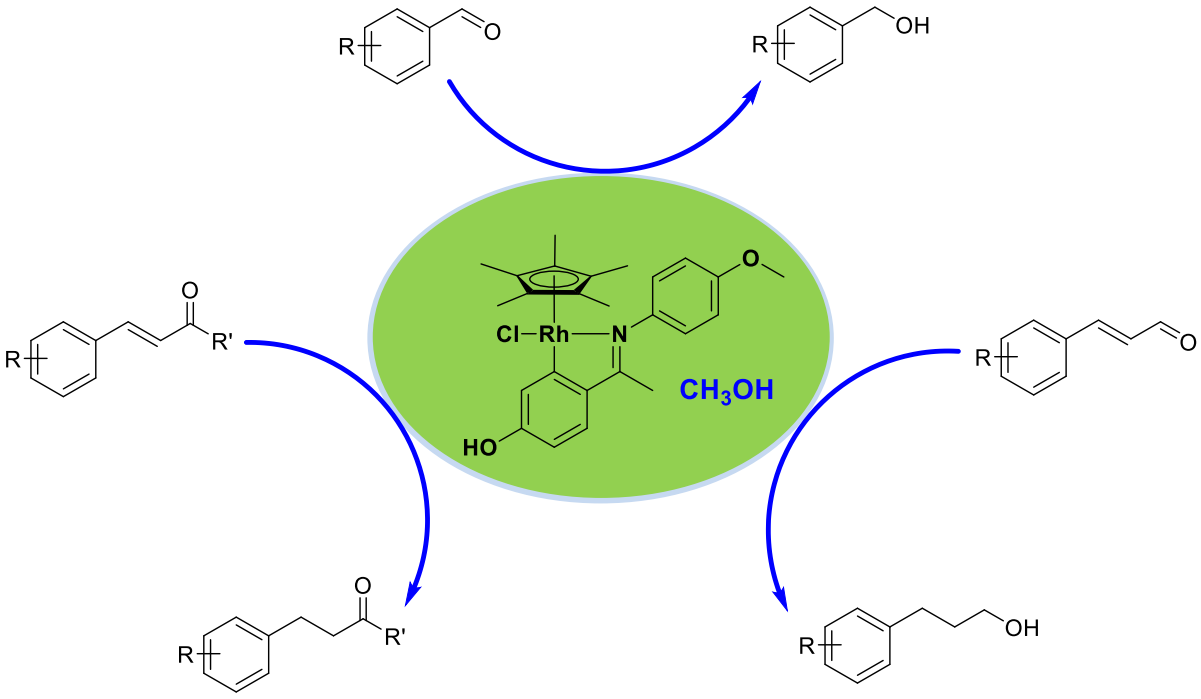
Conclusion and Perspectives

Conclusion and Perspectives

This thesis describes the synthesis, characterisation and investigation of new rhodium complexes for the selective TH of aldehydes and α,β-unsaturated carbonyl compounds. Although these types of reductions have been widely studied by many research groups, there are still some limitations and challenges, especially for the chemoselective reduction of aldehydes and α,β-unsaturated carbonyl compounds with the use of inexpensive and easy-to-handle reagents that provide milder reaction conditions with no need for inert gas protection.

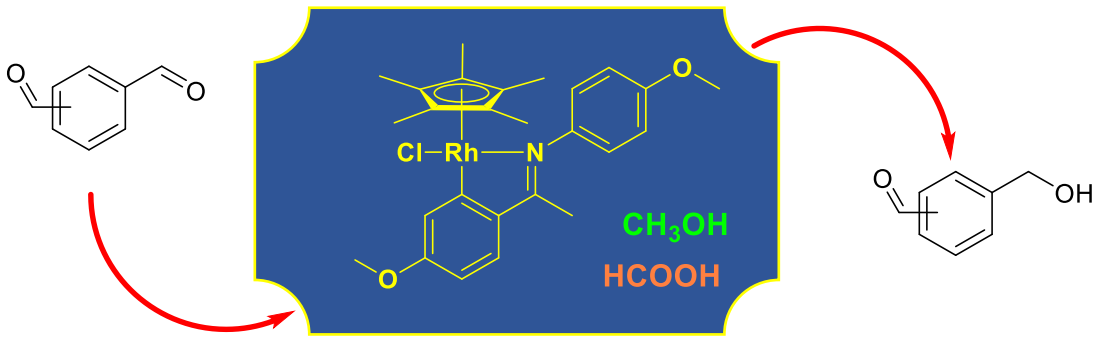
The newly synthesised rhodium complexes have been found to be highly efficient, chemoselective and operationally simple with a broad substrate scope and functional group tolerance in the field of TH. Of particular note is that the reduction is performed using abundant methanol as both the reaction solvent and source of hydrogen. In addition, the reaction is carried out in an open atmosphere which provides a step forward to an efficient, greener, and benign reaction. Moreover, the replacement of the -OCH_3 group in the imine ligand in the rhodium complex with the more electron rich -OH one shows a significant difference in the TH process by lowering the catalyst loading by half and completing the reaction in a shorter period.

Further, this system provides a new and remarkable synthetic route that has never been previously reported for α,β-unsaturated ketones by tolerating the C=O double bond in the presence of a variety of sensitive functionalities utilising methanol as the hydrogen donor and solvent. On the other hand, the rhodium complex is capable of reducing both C=C and C=O double bonds in α,β-unsaturated aldehydes, providing fully saturated alcohol at room temperature. In fact, the rhodium complex is considered to be the first example that performs methanol dehydrogenation under ambient conditions. Such a transformation is highly desirable in terms of economy. Scheme 6.1 summarise the various TH reactions described in this thesis.



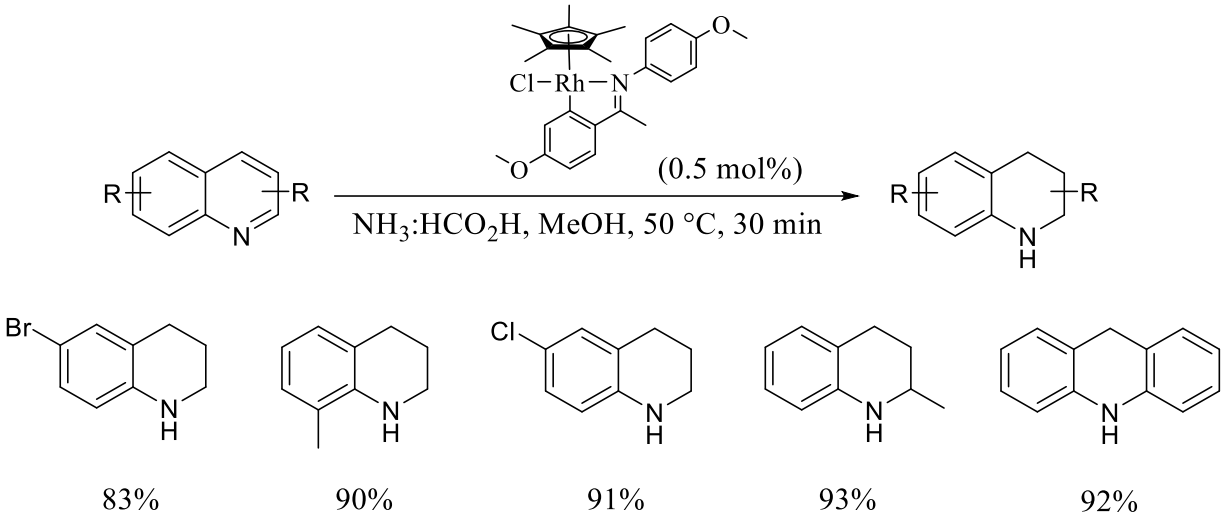
Scheme 6.1: Summary of the research TH reduction using methanol as reaction solvent/hydrogen donor

Rhodium complex **A_1** has also been found to be viable for the selective reduction of a wide range of mono- as well as di-aldehydes. Using an azeotropic formic acid and triethylamine mixture, this complex reduces di-aldehydes selectively providing the highly important hydroxymethyl aldehydes for the agrochemical, pharmaceutical, and fine chemical industries. A summary of the TH of mono- and di-aldehydes is shown in Scheme 6.2.



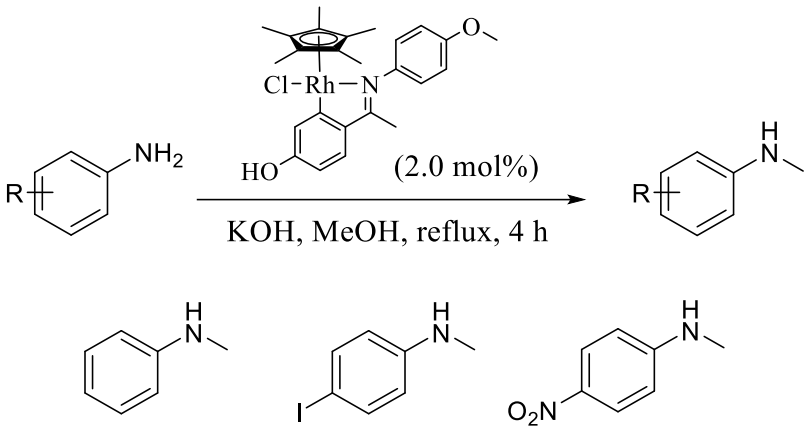
Scheme 6.2: Summary of the research covered in the reduction of mono- and di-aldehydes

The rhodium complex has also shown potential towards the TH of a range of quinolines. This reaction is easy to perform and gives a useful method for the production of 1,2,3,4-tetrahydroquinoline derivatives from readily available quinolines. Preliminary results for this reduction are shown in Scheme 6.3, which are not described in the previous Chapters.

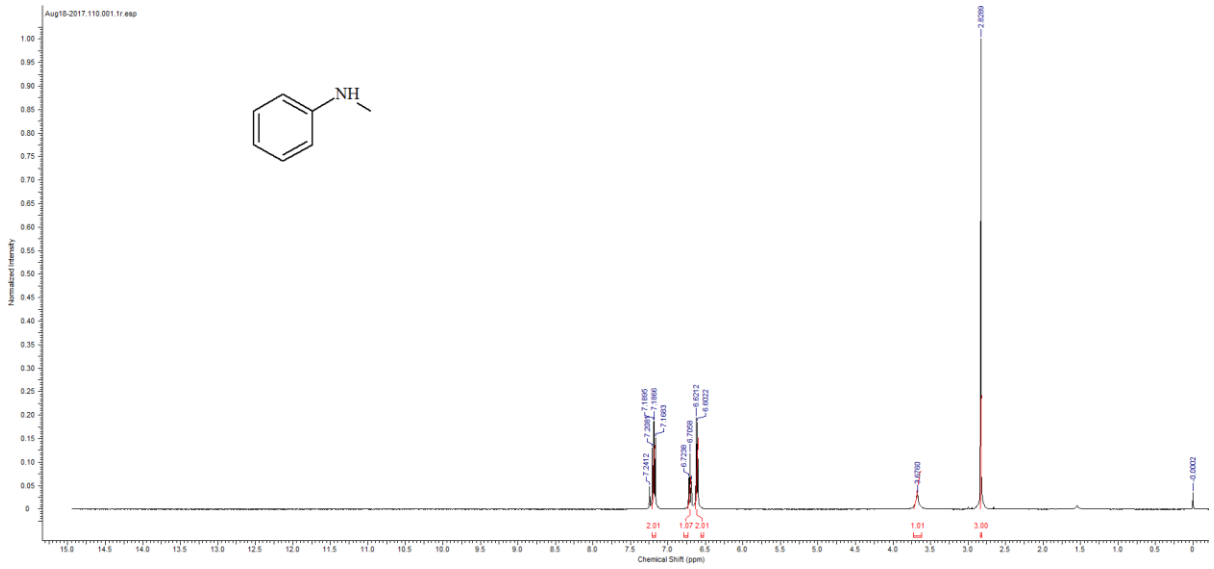


Scheme 6.3: Preliminary results for the TH of quinolones

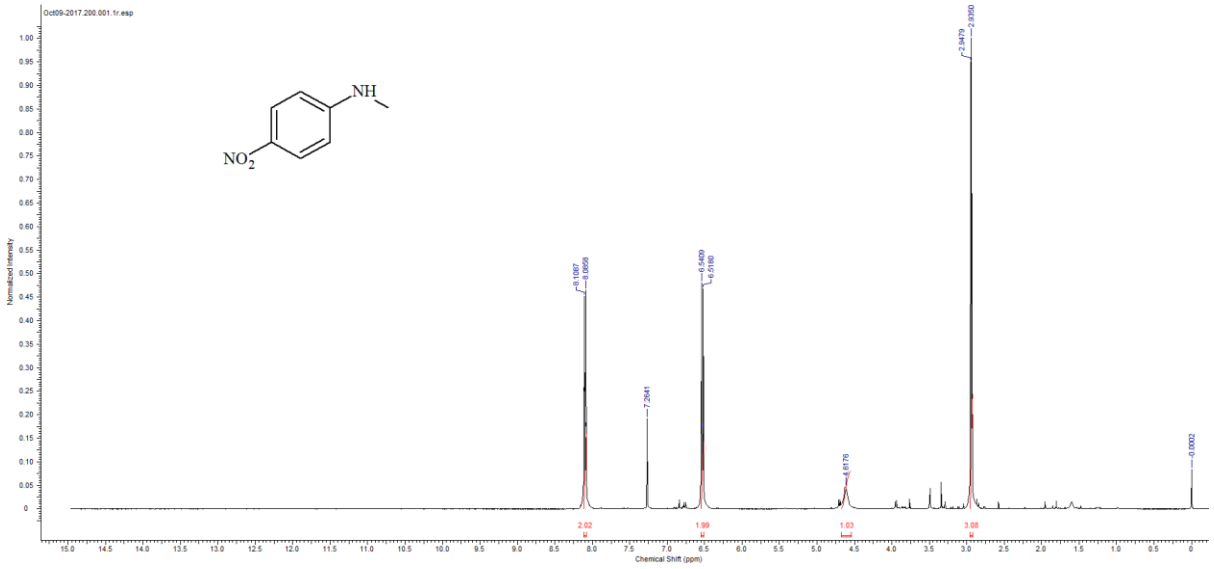
In the area of hydrogen borrowing reactions, the complex has presented promising catalytic ability using methanol as a sustainable C1 source for mono-methylation of aniline compounds. Preliminary results for this reaction show that the catalyst is highly selective and efficient for the monoalkylation of substituted anilines under normal conditions. The crude ^{1}H-NMR results clearly show the reaction is clean, which can be considered as a waste-free reaction. Examples of anilines used in this work and ^{1}H-NMR data for their products are shown in Schemes 6.4 and 6.4a-c.



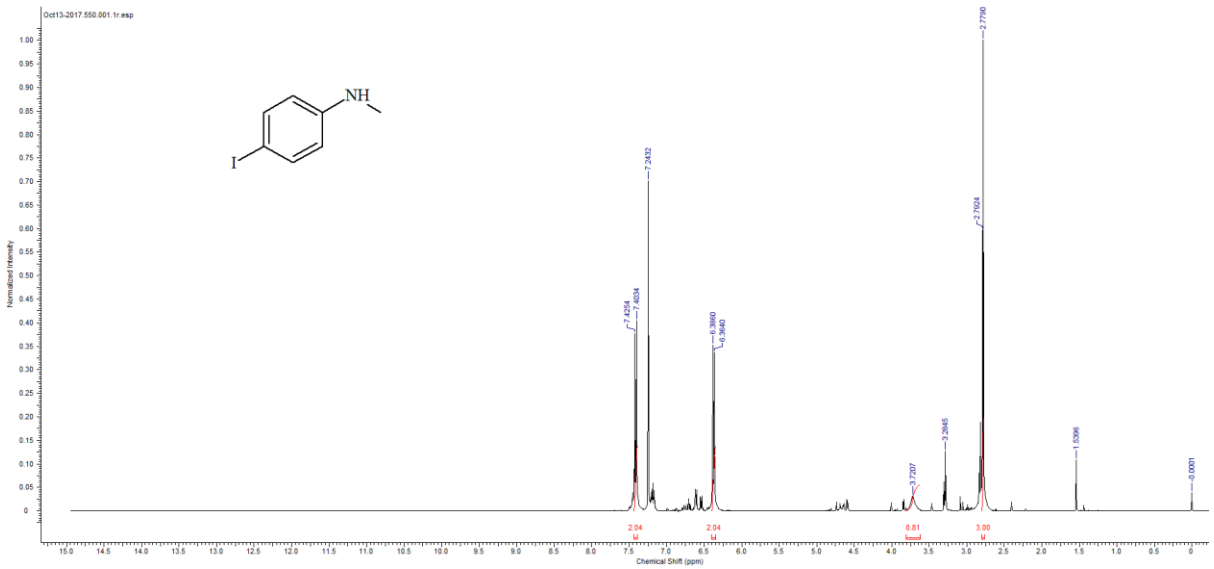
Scheme 6.4: Examples of methylation of anilines



Scheme 6.4a: ^{1}H-NMR spectrum of the crude product from methylation of aniline



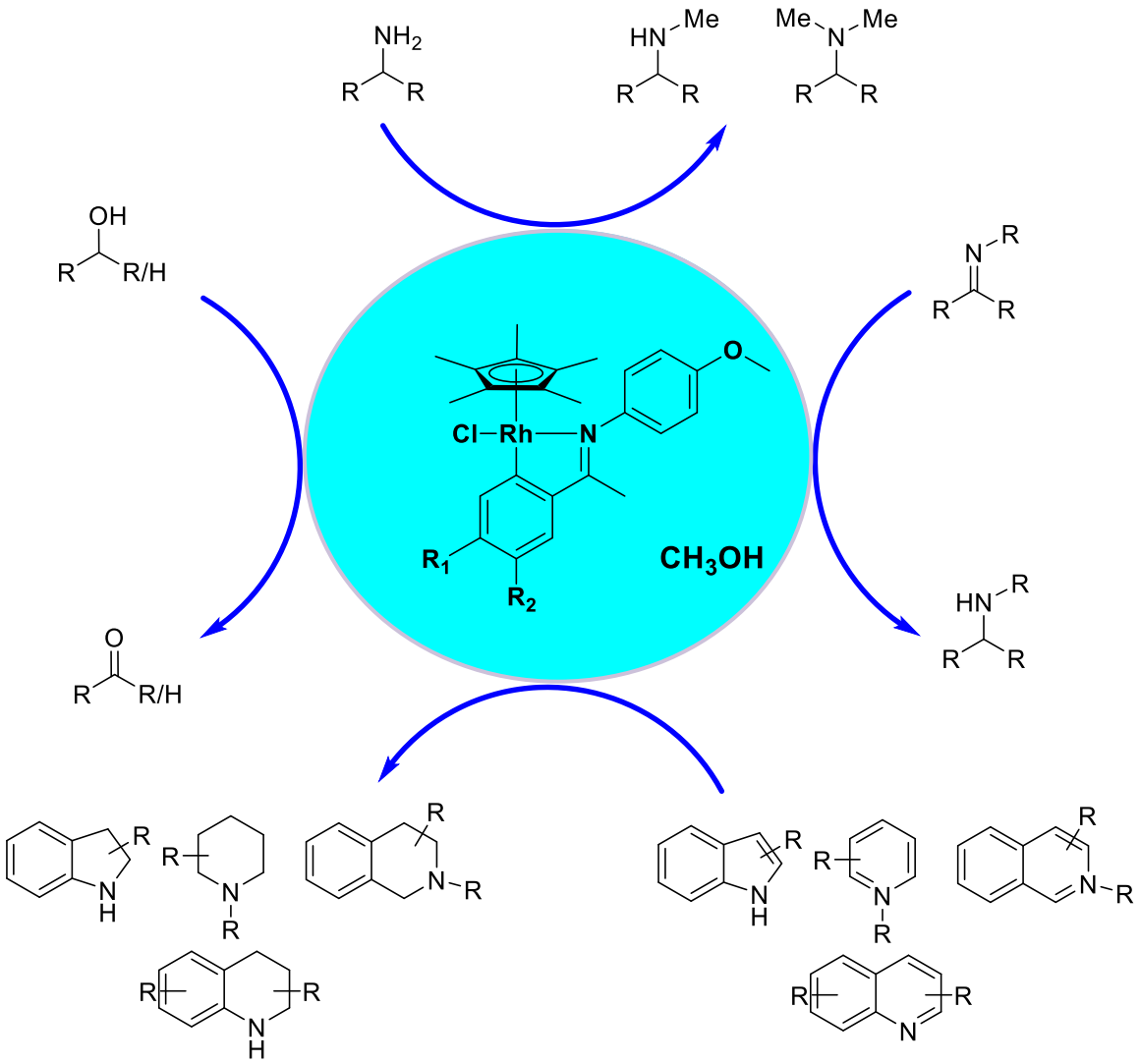
Scheme 6.4b: ^{1}H-NMR spectrum of the crude product from methylation of 4-nitroaniline



Scheme 6.4c: ^{1}H-NMR spectrum of the crude product from methylation of 4-iodoaniline

It is hoped that the work presented in this thesis has provided some clues to overcome the challenges associated with the use of methanol as a hydrogen donor and a reaction solvent for the clean TH of aldehydes and α,β-unsaturated carbonyl compounds. Future work could involve the development of new complexes that are capable of the selective reduction of heterocyclic and imine compounds and also the selective mono- or di-methylation of amines. Furthermore, these complexes could be applied to other catalytic reactions, for example,

alcohol dehydrogenation to aldehydes or ketones. These tasks might be targeted by modifying the imine ligands by introducing -OH or -NH_2 group in *meta* or in both *meta* and *para* positions to the metal centre, which might be helpful for accessing such transformations. A summary of future work is shown in Scheme 6.5.



1. R_1=H, R_2=OH, **2.** R_1=OH, R_2=OH, **3.** R_1=NH_2, R_2=H, **4.** R_1=H, R_2=NH_2,

5. R_1=NH_2, R_2=NH_2, **6.** R_1=OH, R_2=NH_2, **7.** R_1=NH_2, R_2=OH

Scheme 6.5: Summary of possible future work with the designed rhodium complexes

APPENDIX

Table S.1: Crystal data and structure refinement for catalyst **A_7**

Identification code	**A_7**
Empirical formula	$C_{25}H_{29}ClNO_2Rh$
Formula weight	513.85
Temperature/K	100
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	8.6375(3)
b/Å	13.8673(4)
c/Å	18.4717(6)
α/°	90.00
β/°	103.076(3)
γ/°	90.00
Volume/Å^3	2155.15(12)
Z	4
ρ_{calc}g/cm^3	1.584
μ/mm^{-1}	0.939
F(000)	1056.0
Crystal size/mm^3	0.03 × 0.02 × 0.005
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	3.7 to 52.74
Index ranges	$-10 \leq h \leq 10$, $-17 \leq k \leq 17$, $-22 \leq l \leq 23$
Reflections collected	34723
Independent reflections	4406 [R_{int} = 0.1371, R_{sigma} = 0.0711]
Data/restraints/parameters	4406/0/279
Goodness-of-fit on F^2	1.063
Final R indexes [I>=2σ (I)]	R_1 = 0.0477, wR_2 = 0.0794
Final R indexes [all data]	R_1 = 0.0673, wR_2 = 0.0868
Largest diff. peak/hole / e Å^{-3}	0.59/-0.62

Table S.2: Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for **A7**. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor

Atom	*X*	*y*	*z*	U(eq)
Rh1	3711.8(4)	6670.3(2)	6618.40(18)	11.62(9)
Cl1	1216.2(12)	7489.9(7)	6154.1(6)	16.9(2)
O1	502(3)	3516(2)	5347.0(16)	18.2(7)
O2	7497(4)	10837(2)	5855.1(17)	21.3(7)
N1	4573(4)	7229(2)	5727.2(18)	12.3(7)
C2	3387(5)	5840(3)	5146(2)	14.2(9)
C1	4260(5)	6726(3)	5111(2)	14.3(9)
C5	1456(5)	4269(3)	5259(2)	14.5(9)
C8	4677(5)	7044(3)	4403(2)	16.8(9)
C3	2946(5)	5665(3)	5828(2)	12.2(9)
C4	1988(5)	4875(3)	5871(2)	13.4(9)
C6	1927(5)	4438(3)	4594(2)	16.1(9)
C10	4661(5)	8953(3)	5965(2)	15.4(9)
C20	3652(5)	6995(3)	7797(2)	14.4(9)
C9	5401(5)	8133(3)	5770(2)	13.2(9)
C19	3559(5)	5972(3)	7647(2)	15.1(9)
C13	7668(5)	9098(3)	5660(2)	16.6(9)
C18	5009(5)	5693(3)	7452(2)	14.5(9)
C12	6896(5)	9920(3)	5824(2)	15.5(9)
C7	2878(5)	5212(3)	4543(2)	15.6(9)
C11	5401(5)	9837(3)	5984(2)	17.4(9)
C24	2306(5)	5325(3)	7809(2)	20.8(10)
C17	5930(5)	6551(3)	7442(2)	14.0(9)
C14	6913(5)	8206(3)	5639(2)	18.4(10)
C15	8886(5)	10979(3)	5572(2)	22.6(10)
C25	2409(5)	7549(3)	8059(2)	20.7(10)
C16	5110(5)	7349(3)	7686(2)	15.0(9)
C22	7575(5)	6592(3)	7309(2)	20.4(10)
C21	5743(5)	8349(3)	7830(2)	21.4(10)
C23	5485(5)	4675(3)	7336(3)	21.3(10)

Table S.3: Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for **A7**. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Rh1	12.87(18)	11.48(16)	10.11(16)	-0.75(15)	1.77(12)	-0.16(14)
Cl1	14.5(5)	17.0(5)	17.9(5)	-1.2(4)	1.2(4)	1.6(4)
O1	21.8(17)	17.4(16)	14.0(16)	-3.7(13)	1.2(13)	-4.9(13)
O2	24.6(18)	15.5(16)	24.6(18)	-2.2(14)	7.6(14)	-5.6(13)
N1	14.6(19)	12.1(17)	11.3(19)	2.7(15)	5.2(14)	1.3(14)
C2	12(2)	14(2)	17(2)	-1.0(18)	2.6(17)	3.1(17)
C1	11(2)	18(2)	14(2)	3.2(19)	2.0(16)	4.6(18)
C5	10(2)	9(2)	22(2)	2.1(18)	-1.2(17)	2.5(16)
C8	17(2)	17(2)	16(2)	-0.1(19)	2.5(18)	-3.0(18)
C3	11(2)	12(2)	13(2)	-2.3(18)	1.5(16)	3.9(16)
C4	15(2)	13(2)	11(2)	0.8(18)	2.5(16)	1.4(17)
C6	19(2)	14(2)	14(2)	-3.5(18)	0.9(17)	3.9(18)
C10	15(2)	20(2)	11(2)	0.6(18)	4.9(17)	-2.5(18)
C20	19(2)	16(2)	5(2)	-0.1(17)	-2.3(16)	2.2(17)
C9	14(2)	13(2)	12(2)	2.3(17)	4.0(16)	0.8(16)
C19	20(2)	16(2)	8(2)	1.4(18)	1.3(17)	-0.4(18)
C13	13(2)	19(2)	17(2)	-1.0(19)	2.8(17)	-5.1(18)
C18	20(2)	14(2)	9(2)	-0.3(18)	2.3(17)	0.1(18)
C12	23(2)	16(2)	8(2)	2.1(18)	2.4(17)	-4.5(18)
C7	16(2)	19(2)	13(2)	-1.9(18)	6.2(17)	3.7(18)
C11	22(3)	17(2)	14(2)	-0.7(19)	5.4(18)	3.0(19)
C24	26(3)	18(2)	20(2)	2(2)	8(2)	-5.9(19)
C17	8(2)	24(2)	8(2)	5.4(18)	-2.7(15)	-0.1(18)
C14	22(2)	15(2)	17(2)	0.9(19)	1.6(18)	3.0(19)
C15	25(3)	24(2)	19(2)	2(2)	5.0(19)	-9(2)
C25	22(3)	24(3)	16(2)	-5(2)	3.4(19)	3(2)
C16	16(2)	19(2)	7(2)	-0.9(18)	-2.4(16)	0.5(18)
C22	16(2)	28(2)	16(2)	1(2)	2.6(17)	2(2)
C21	20(2)	20(2)	22(2)	-1(2)	-0.2(18)	-5(2)
C23	28(3)	14(2)	22(3)	1.0(19)	5(2)	6.5(19)

Table S.4: Bond Lengths for **A_7**

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Rh1	Cl1	2.4160(10)	C3	C4	1.386(5)
Rh1	N1	2.102(3)	C6	C7	1.368(6)
Rh1	C3	2.019(4)	C10	C9	1.392(5)
Rh1	C20	2.235(4)	C10	C11	1.379(6)
Rh1	C19	2.163(4)	C20	C19	1.444(6)
Rh1	C18	2.164(4)	C20	C25	1.487(6)
Rh1	C17	2.166(4)	C20	C16	1.409(6)
Rh1	C16	2.270(4)	C9	C14	1.384(6)
O1	C5	1.363(5)	C19	C18	1.433(6)
O2	C12	1.370(5)	C19	C24	1.488(6)
O2	C15	1.427(5)	C13	C12	1.388(6)
N1	C1	1.310(5)	C13	C14	1.395(6)
N1	C9	1.436(5)	C18	C17	1.433(6)
C2	C1	1.451(6)	C18	C23	1.499(5)
C2	C3	1.416(6)	C12	C11	1.393(6)
C2	C7	1.403(6)	C17	C16	1.440(6)
C1	C8	1.499(5)	C17	C22	1.497(6)
C5	C4	1.400(6)	C16	C21	1.491(6)
C5	C6	1.398(6)			

Table S.5: Bond Angles for **A_7**

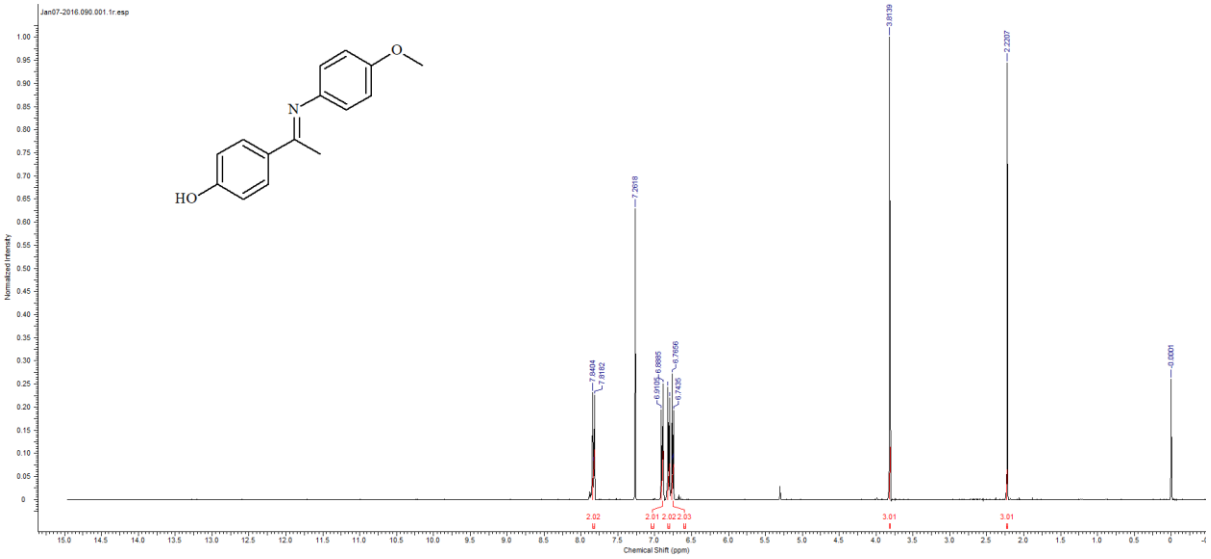
Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
N1	Rh1	Cl1	89.66(9)	C3	C4	C5	121.3(4)
N1	Rh1	C20	141.14(14)	C7	C6	C5	119.3(4)
N1	Rh1	C19	162.89(14)	C11	C10	C9	119.8(4)
N1	Rh1	C18	124.76(14)	C19	C20	Rh1	68.2(2)
N1	Rh1	C17	99.47(14)	C19	C20	C25	123.8(4)
N1	Rh1	C16	108.30(15)	C25	C20	Rh1	126.8(3)
C3	Rh1	Cl1	87.03(11)	C16	C20	Rh1	73.1(2)
C3	Rh1	N1	78.71(15)	C16	C20	C19	109.1(4)
C3	Rh1	C20	140.16(16)	C16	C20	C25	127.0(4)
C3	Rh1	C19	104.56(16)	C10	C9	N1	118.4(4)
C3	Rh1	C18	96.59(15)	C14	C9	N1	122.1(4)
C3	Rh1	C17	123.24(16)	C14	C9	C10	119.4(4)
C3	Rh1	C16	159.61(15)	C20	C19	Rh1	73.5(2)
C20	Rh1	Cl1	92.04(11)	C20	C19	C24	124.5(4)
C20	Rh1	C16	36.44(15)	C18	C19	Rh1	70.7(2)
C19	Rh1	Cl1	107.19(12)	C18	C19	C20	107.4(4)
C19	Rh1	C20	38.29(15)	C18	C19	C24	127.2(4)
C19	Rh1	C18	38.67(15)	C24	C19	Rh1	129.7(3)
C19	Rh1	C17	64.46(15)	C12	C13	C14	119.3(4)
C19	Rh1	C16	63.19(15)	C19	C18	Rh1	70.6(2)
C18	Rh1	Cl1	145.49(12)	C19	C18	C17	107.4(4)
C18	Rh1	C20	63.60(15)	C19	C18	C23	125.0(4)
C18	Rh1	C17	38.65(15)	C17	C18	Rh1	70.8(2)
C18	Rh1	C16	63.49(15)	C17	C18	C23	127.5(4)
C17	Rh1	Cl1	149.47(12)	C23	C18	Rh1	127.0(3)
C17	Rh1	C20	62.81(15)	O2	C12	C13	125.1(4)
C17	Rh1	C16	37.80(15)	O2	C12	C11	115.3(4)
C16	Rh1	Cl1	111.69(11)	C13	C12	C11	119.6(4)
C12	O2	C15	117.1(3)	C6	C7	C2	121.2(4)
C1	N1	Rh1	116.3(3)	C10	C11	C12	120.9(4)
C1	N1	C9	121.0(4)	C18	C17	Rh1	70.6(2)
C9	N1	Rh1	122.6(3)	C18	C17	C16	108.7(4)
C3	C2	C1	115.5(4)	C18	C17	C22	125.7(4)
C7	C2	C1	124.3(4)	C16	C17	Rh1	75.0(2)
C7	C2	C3	120.0(4)	C16	C17	C22	125.1(4)
N1	C1	C2	114.9(4)	C22	C17	Rh1	127.1(3)
N1	C1	C8	123.9(4)	C9	C14	C13	121.0(4)
C2	C1	C8	121.2(4)	C20	C16	Rh1	70.4(2)
O1	C5	C4	117.4(4)	C20	C16	C17	107.2(4)

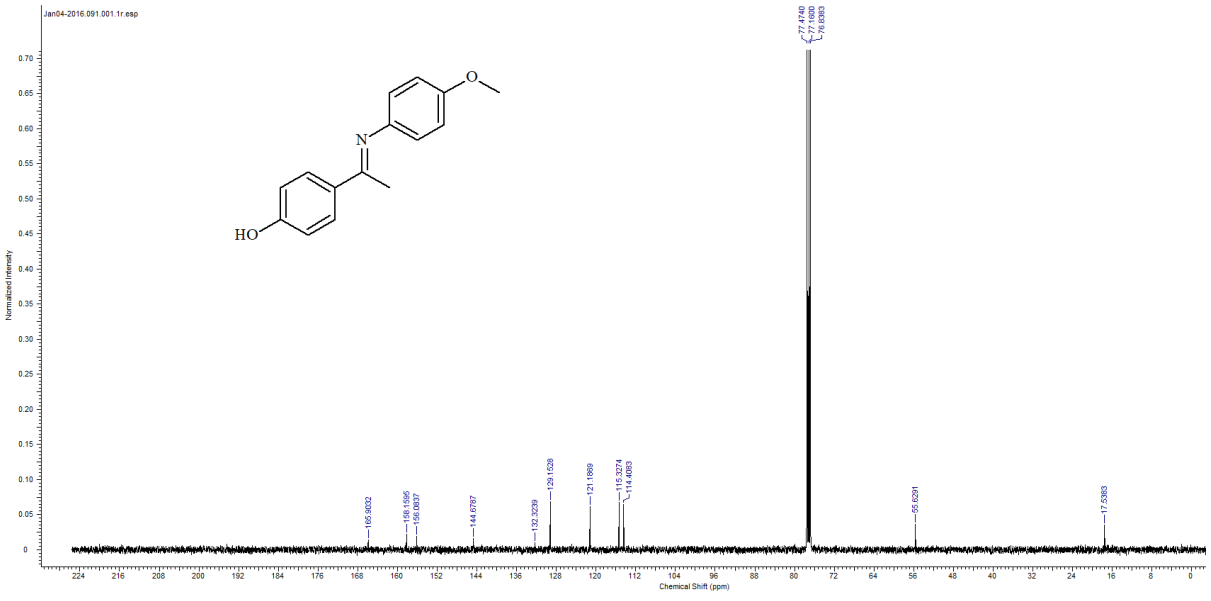
O1	C5	C6	122.5(4)	C20	C16	C21	127.0(4)
C6	C5	C4	120.1(4)	C17	C16	Rh1	67.2(2)
C2	C3	Rh1	114.5(3)	C17	C16	C21	125.7(4)
C4	C3	Rh1	127.3(3)	C21	C16	Rh1	130.0(3)
C4	C3	C2	118.0(4)				

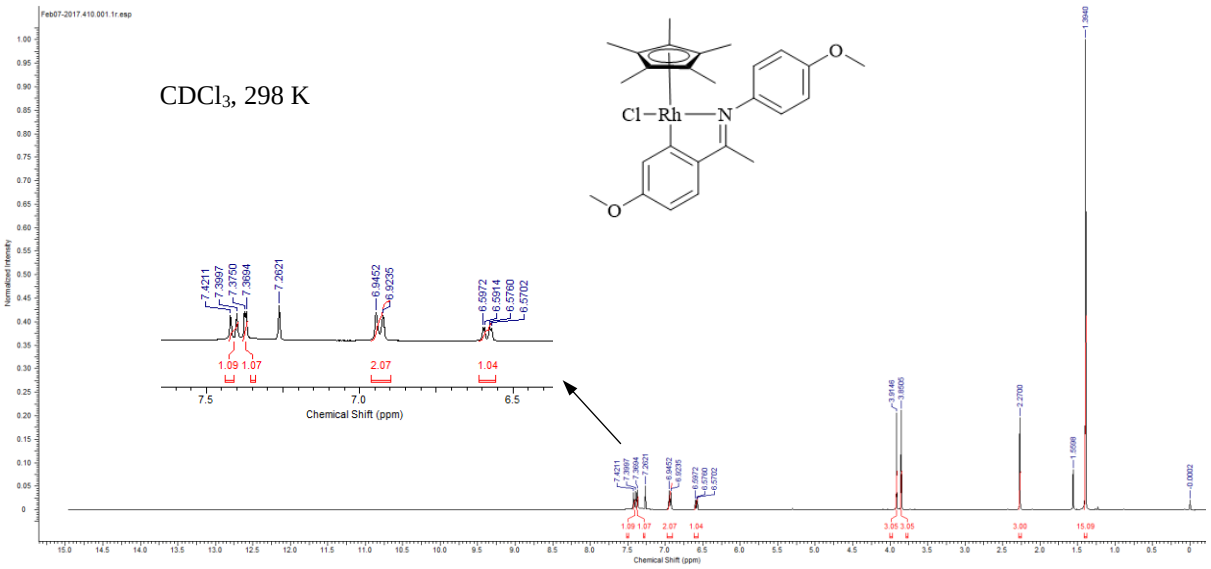
Table S.6: Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for **A$_7$**.

Atom	*X*	*y*	*z*	U(eq)
H1	143	3253	4934	27
H8A	4948	7731	4436	25
H8B	3767	6937	3986	25
H8C	5590	6671	4325	25
H4	1686	4743	6324	16
H6	1589	4019	4181	19
H10	3650	8905	6083	18
H13	8700	9142	5562	20
H7	3200	5327	4092	19
H11	4885	10398	6109	21
H24A	1258	5557	7545	31
H24B	2362	5322	8345	31
H24C	2471	4669	7644	31
H14	7443	7641	5534	22
H15A	8676	10768	5052	34
H15B	9766	10602	5867	34
H15C	9170	11664	5602	34
H25A	2581	8241	8003	31
H25B	2468	7401	8583	31
H25C	1358	7369	7763	31
H22A	7749	6032	7012	31
H22B	8352	6584	7786	31
H22C	7702	7185	7040	31
H21A	6693	8422	7629	32
H21B	6019	8468	8367	32
H21C	4932	8813	7590	32
H23A	4637	4360	6970	32
H23B	5661	4324	7808	32
H23C	6466	4677	7154	32

Copies of NMR Spectra for ligand and rhodium catalysts



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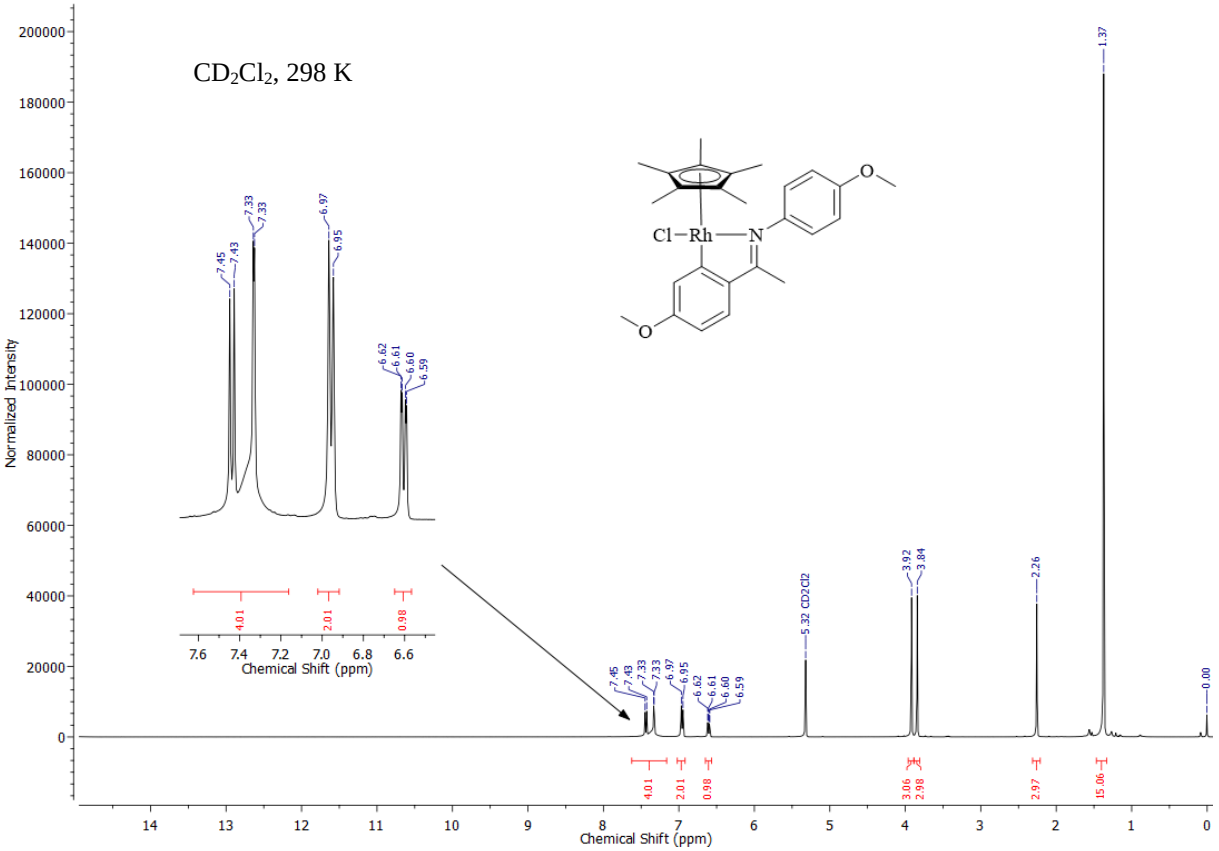
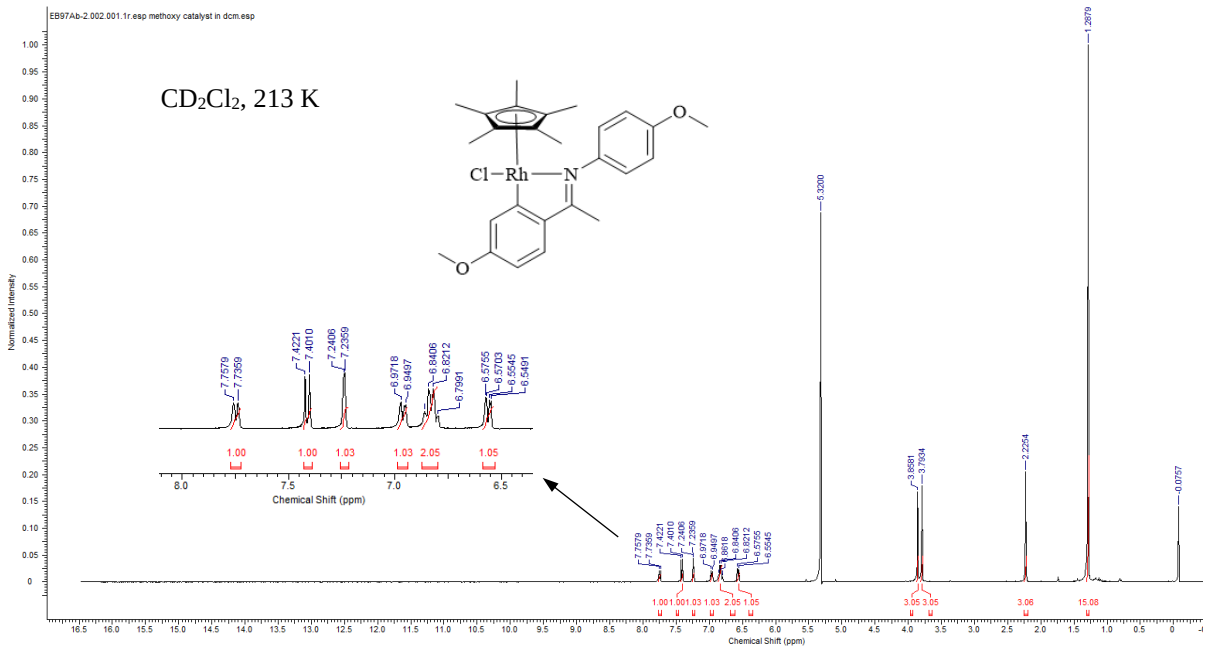
Cl—Rh—N
O
O
Chemical Shift (ppm)


CD2Cl2, 298 K
Cl—Rh—N
O
O
Normalized Intensity
Chemical Shift (ppm)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CD_2Cl_2, 213 K
Cl−Rh−N
O
O
Normalized Intensity
Chemical Shift (ppm)
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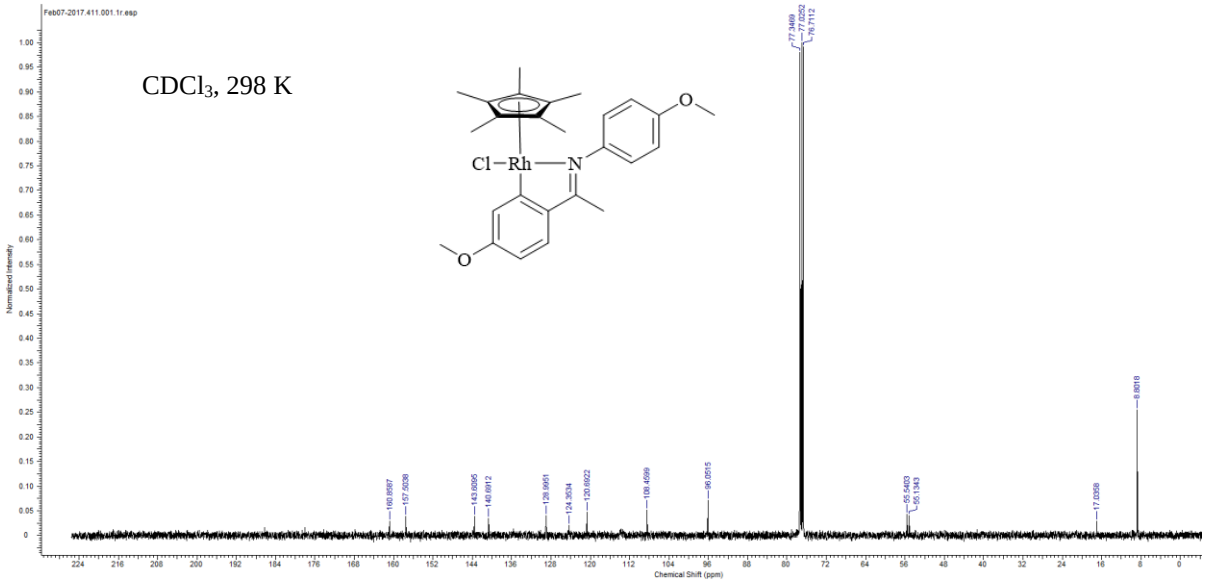
7.7359
7.4221
7.4010
7.2406
7.2359
6.9718
6.9497
6.8406
6.8212
6.7991
6.5755
6.5703
6.5545
6.5491
1.00
1.00
1.03
1.03
2.05
1.05
5.3200
3.8881
3.7934
2.2254
1.2979
0.0757
1.00 1.00 1.03 1.03 2.05 1.05
3.05 3.05
3.06
15.08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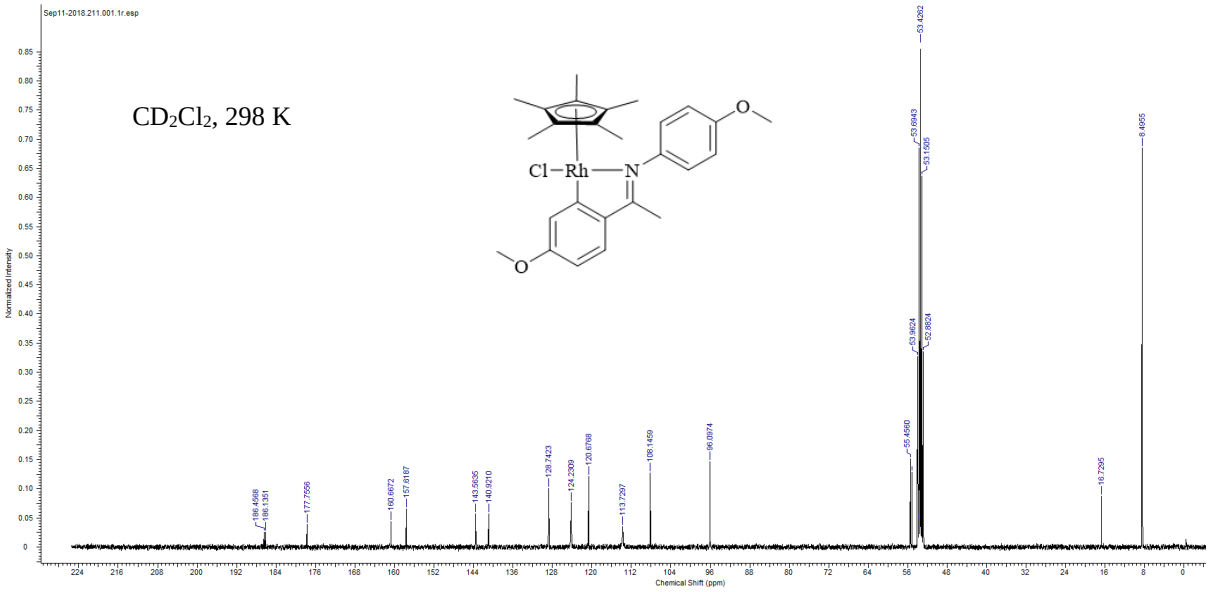
$CDCl_3$, 298 K
Cl−Rh−N
O
O
Normalized Intensity
Chemical Shift (ppm)
77.3499
77.0252
76.7112
160.9587
157.5036
143.6095
140.6912
128.9951
124.3834
120.6922
108.4599
96.0515
55.5403
55.1343
17.0059
8.8018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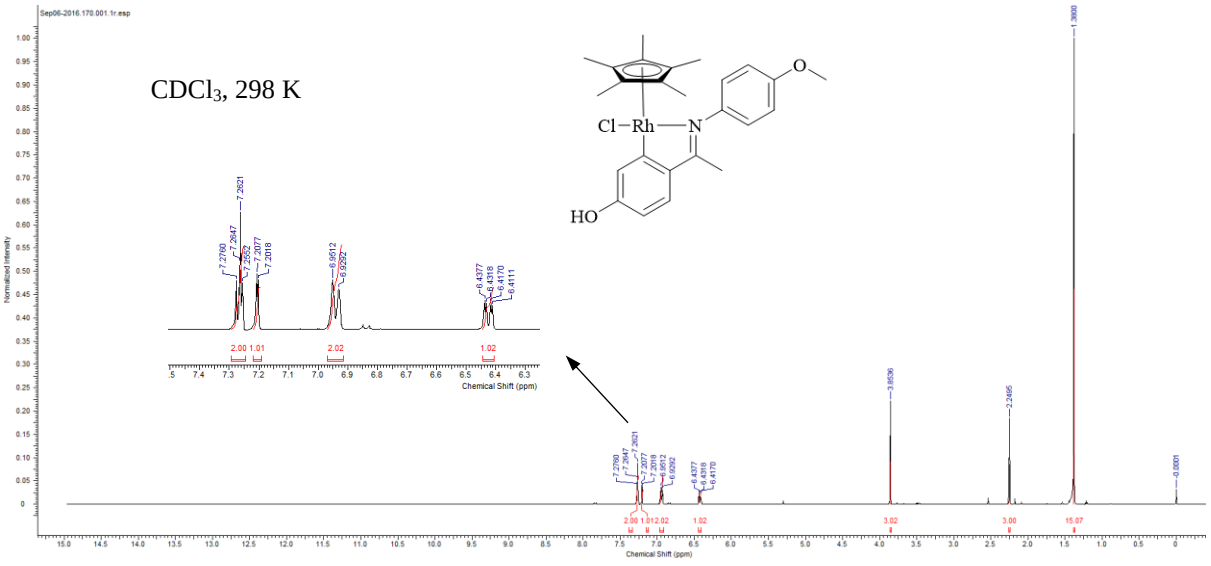
Cl—Rh—N
O
O
Normalized Intensity
Chemical Shift (ppm)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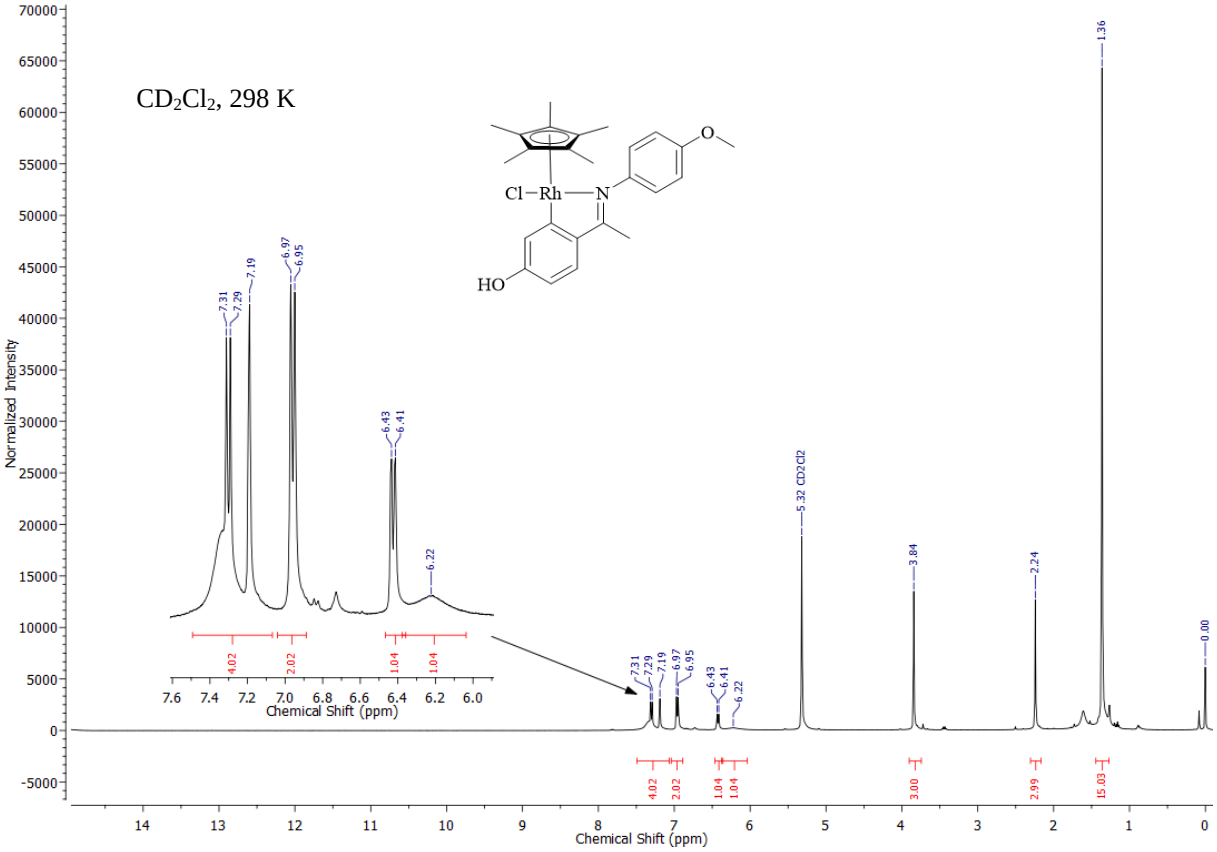
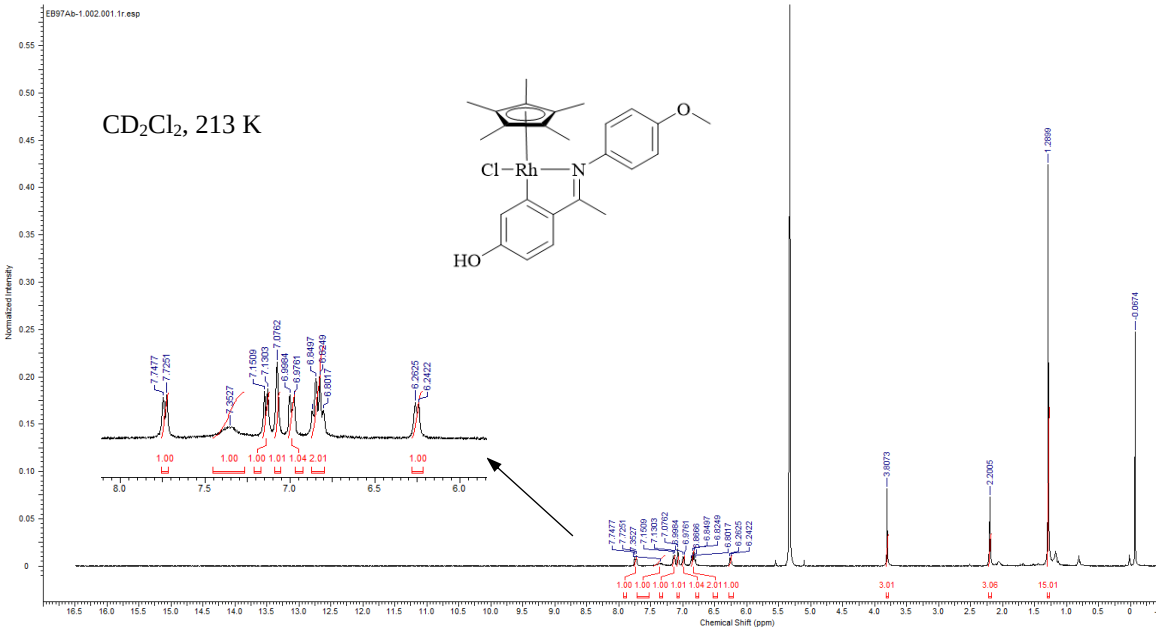
CDCl3, 298 K
Cl—Rh—N
O
HO
Normalized Intensity
Chemical Shift (ppm)


CD2Cl2, 298 K
Cl–Rh–N
O
HO
Normalized Intensity
Chemical Shift (ppm)
7.31
7.29
7.19
6.97
6.95
6.43
6.41
6.22
5.32 CD2Cl2
3.84
2.24
1.36
0.00
4.02
2.02
1.04
1.04
3.00
2.99
15.03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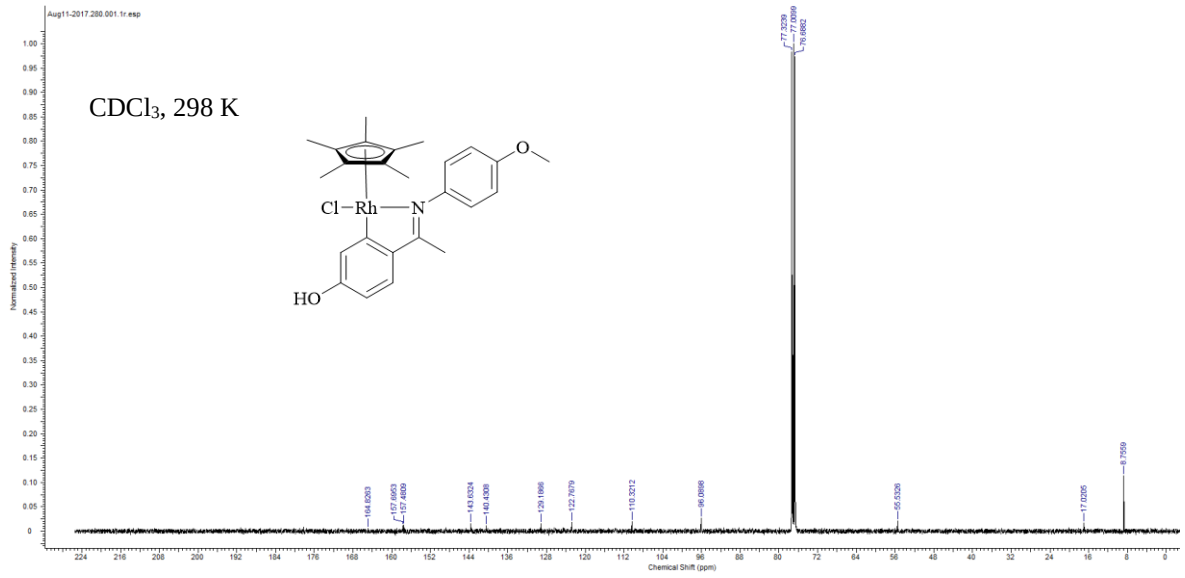
CD2Cl2, 213 K
Cl–Rh–N
O
HO
Normalized Intensity
Chemical Shift (ppm)
7.7477
7.7251
7.3527
7.1509
7.1303
7.0762
6.9984
6.9761
6.8497
6.8249
6.8017
6.2625
6.2422
1.2899
0.0674
3.8073
2.2005
3.01
3.06
15.01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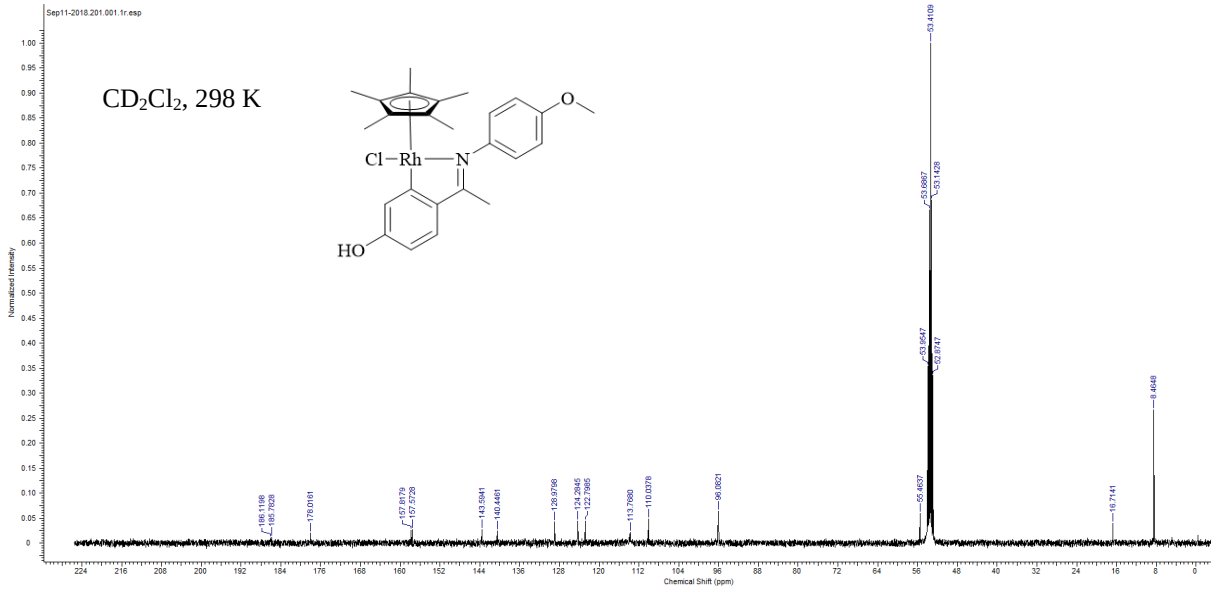
CDCl3, 298 K
Cl−Rh−N
O
HO
Normalized Intensity
Chemical Shift (ppm)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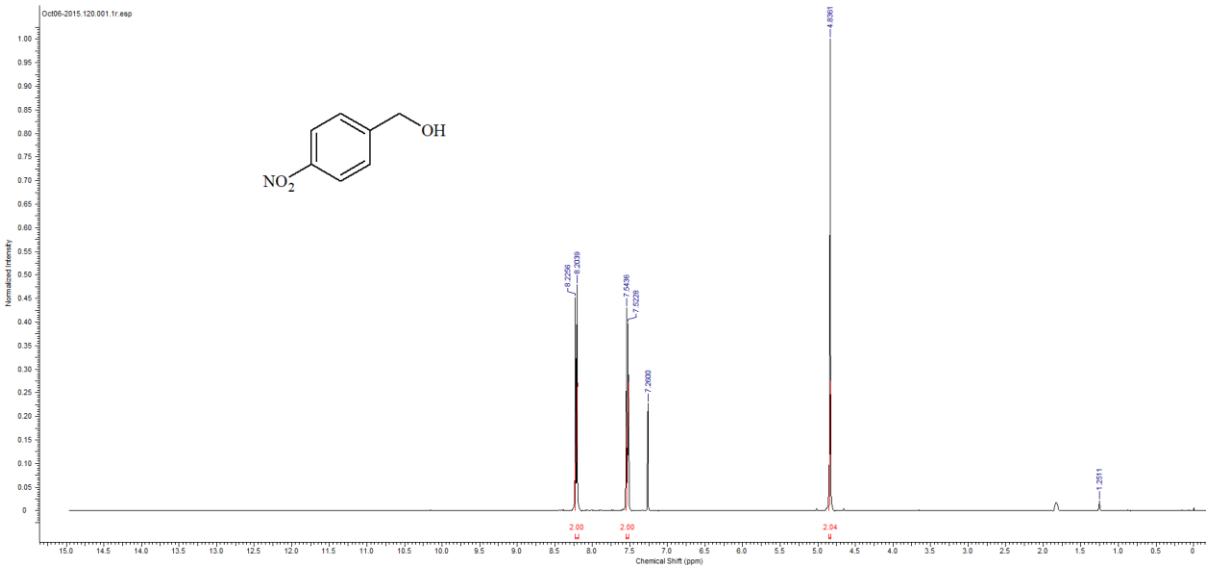
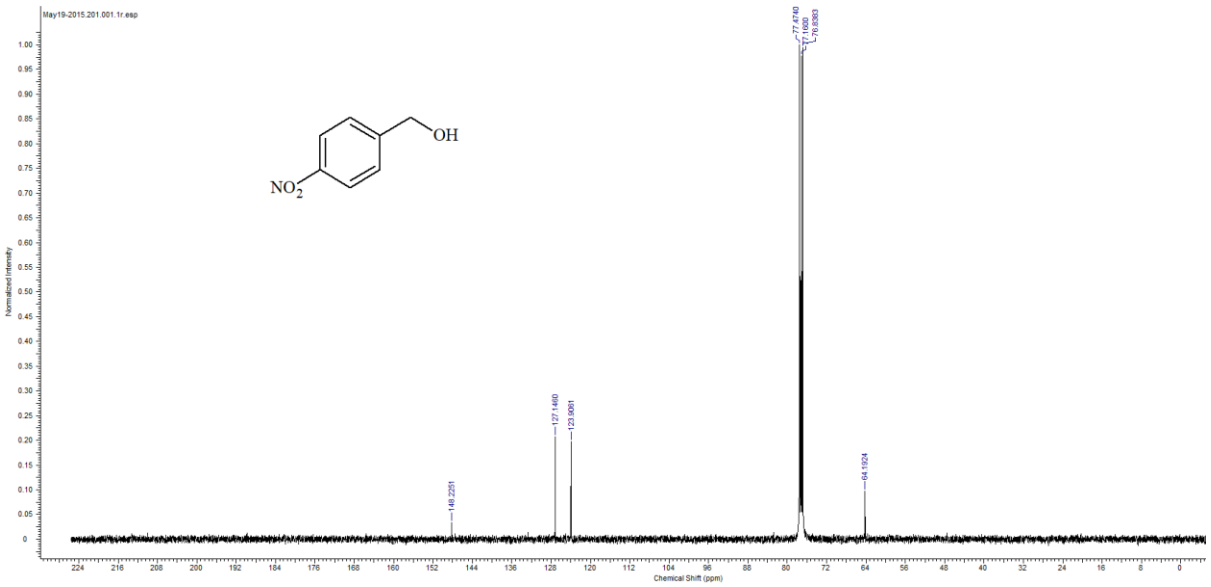
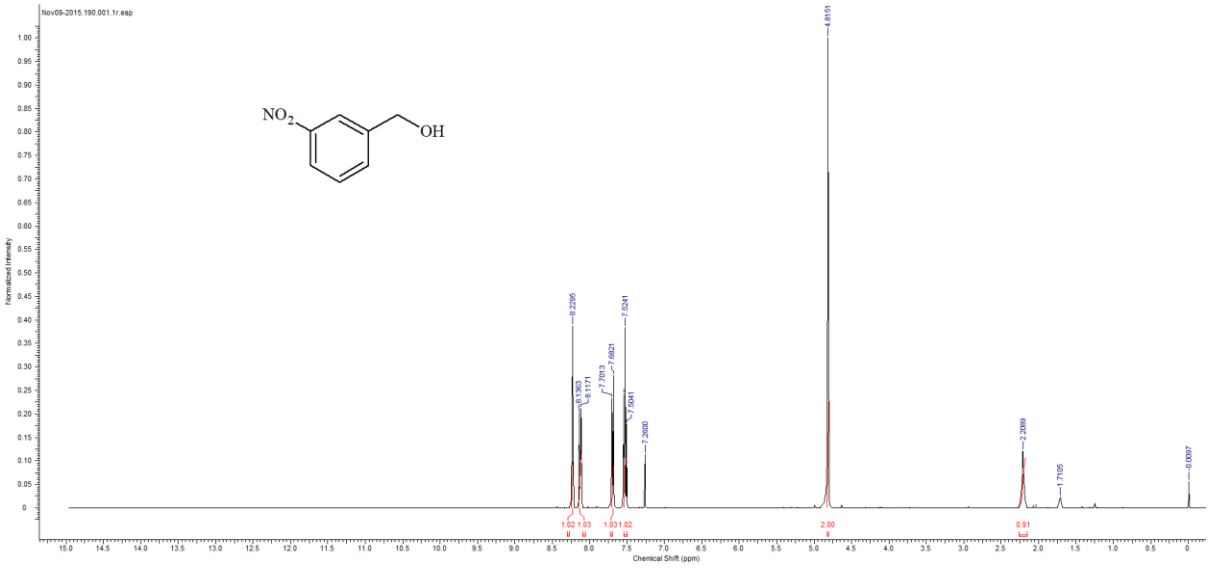
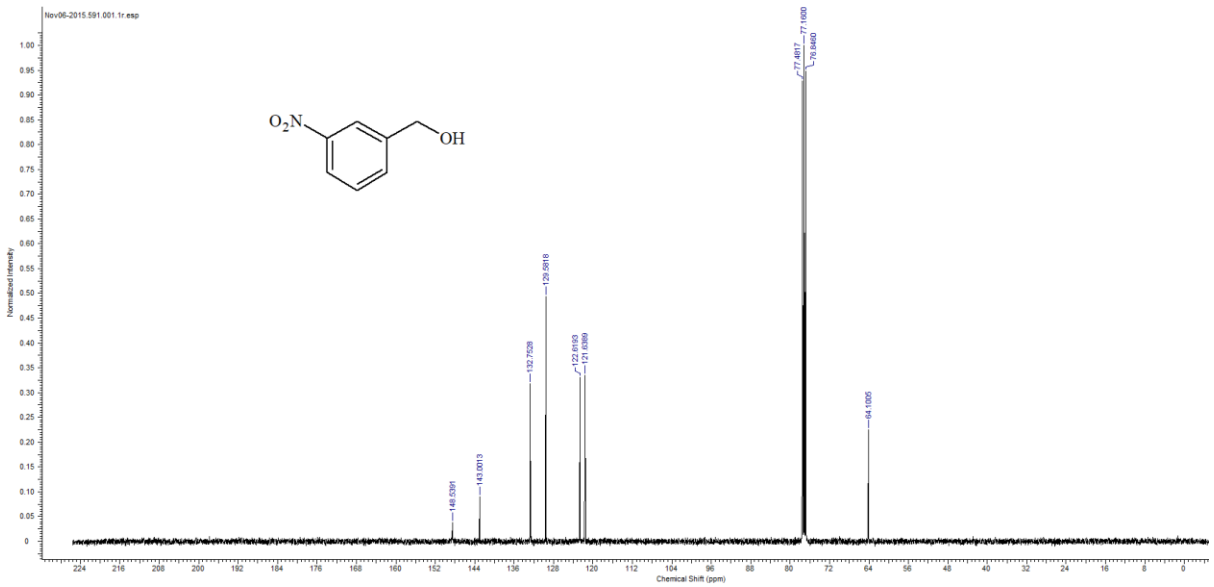
Cl−Rh−N
O
HO
Normalized Intensity
Chemical Shift (ppm)

Copies of NMR Spectra for the reduction of aldehydes with methanol





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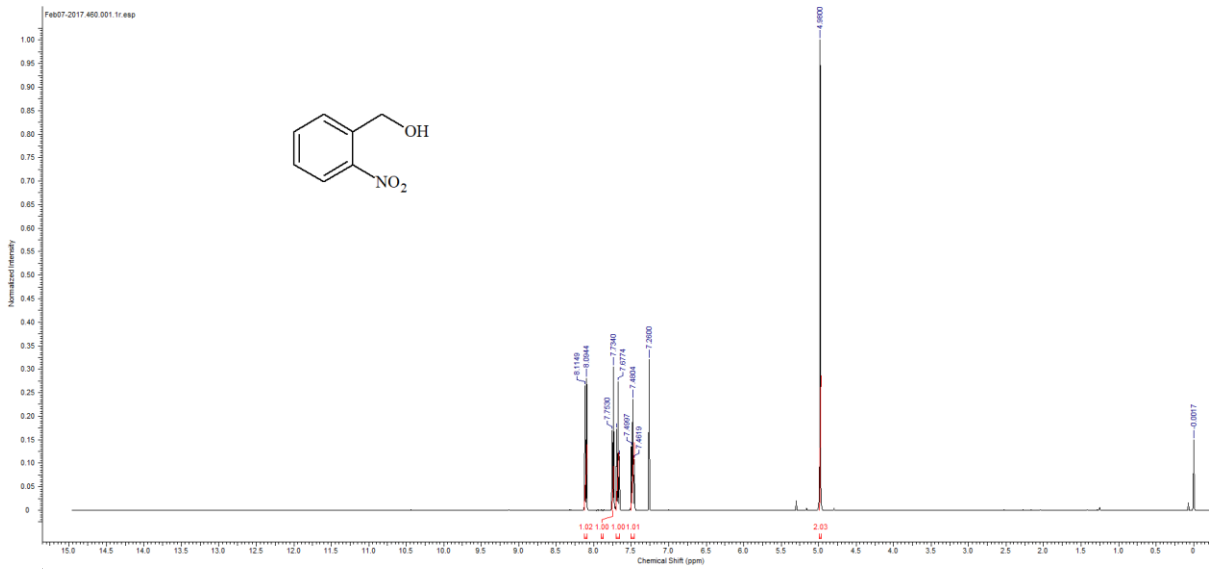
O_2N
OH
Normalized Intensity
Chemical Shift (ppm)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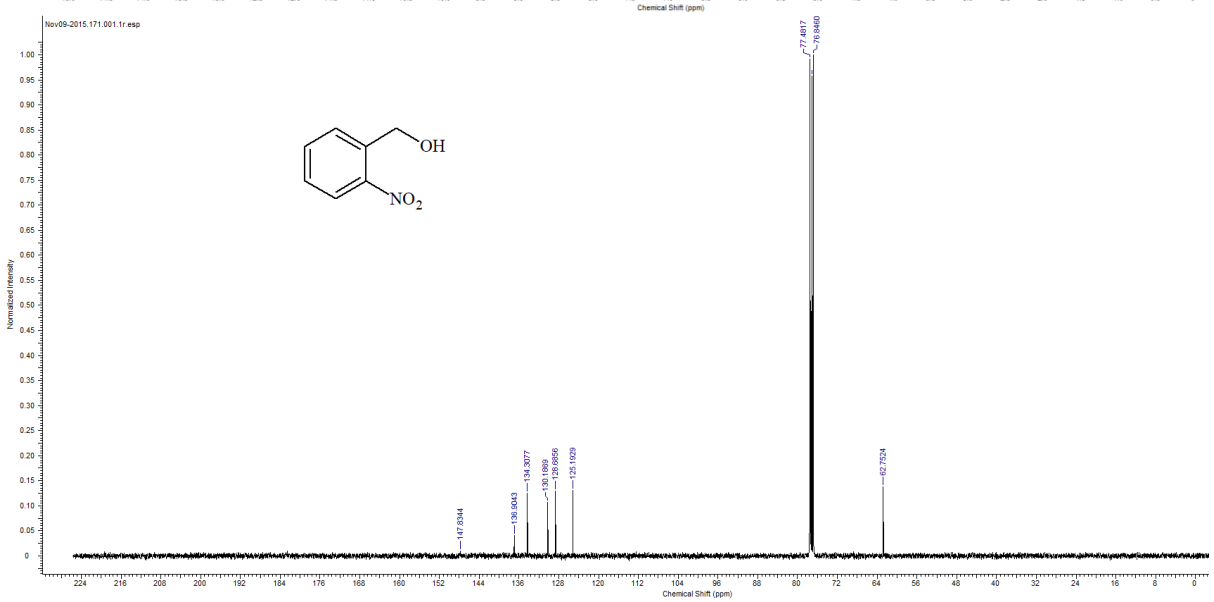
NO_2
Normalized Intensity
Chemical Shift (ppm)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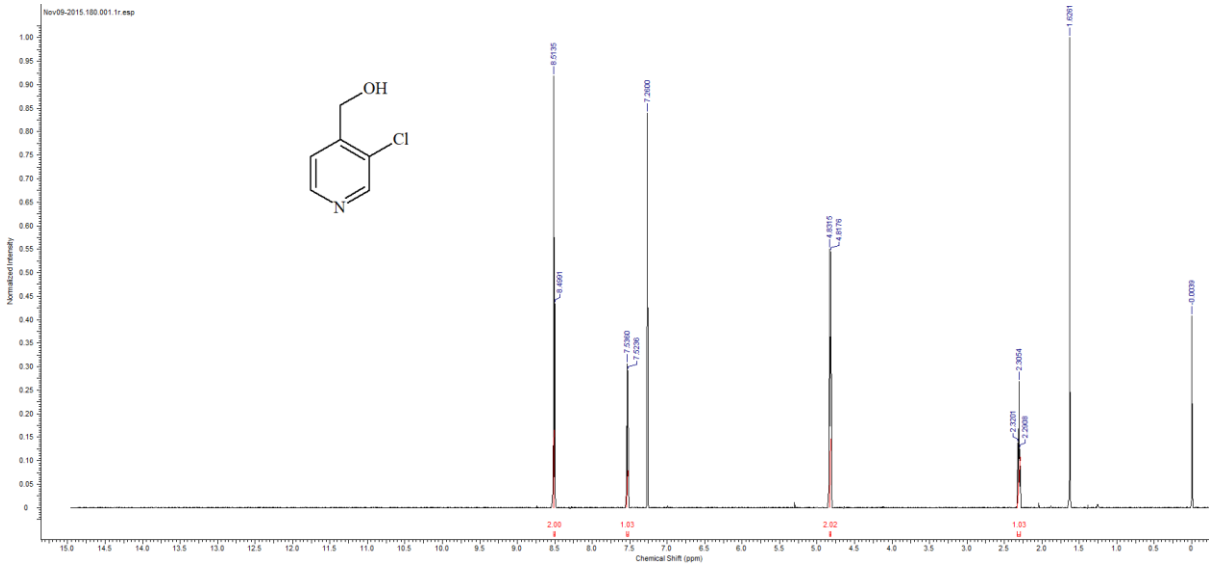
NO_2
Normalized Intensity
Chemical Shift (ppm)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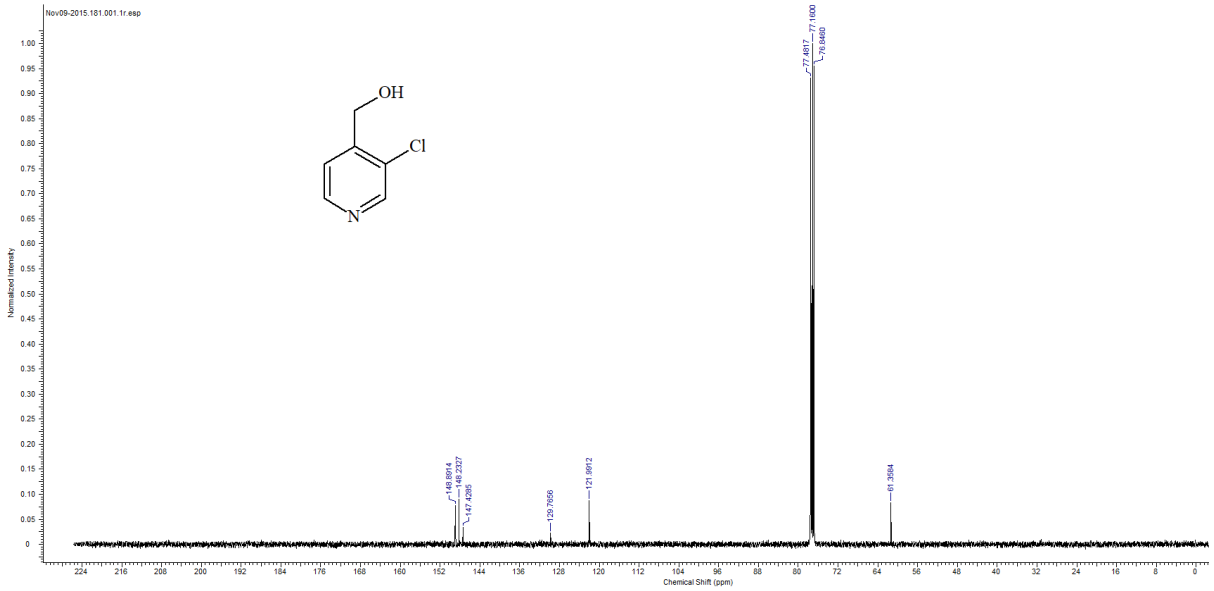
Cl
N
Normalized Intensity
Chemical Shift (ppm)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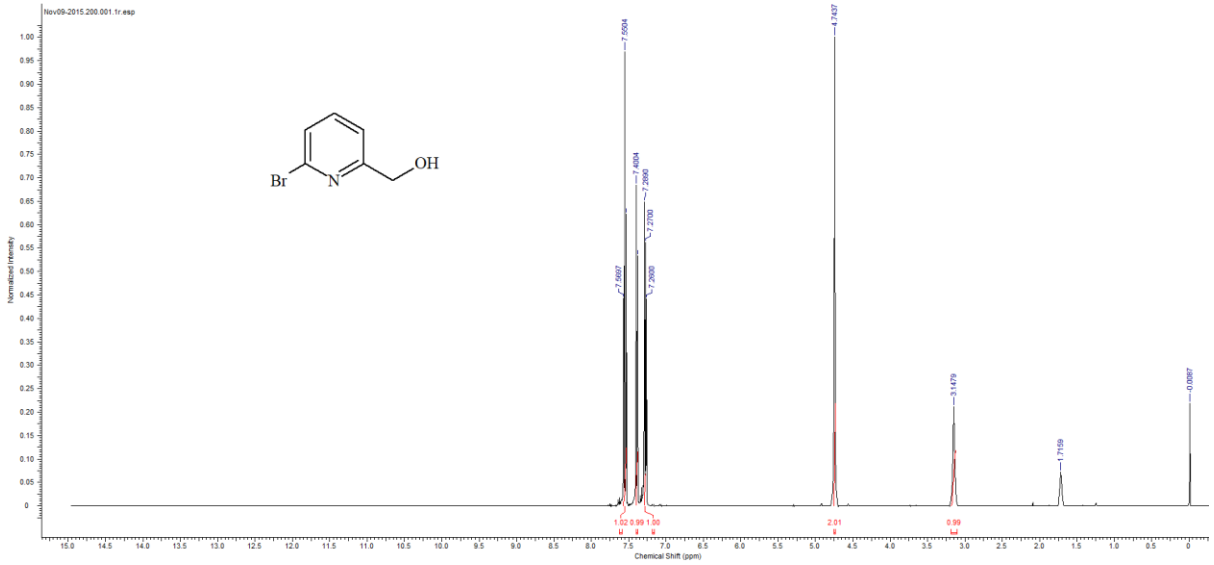
Cl
N
Normalized Intensity
Chemical Shift (ppm)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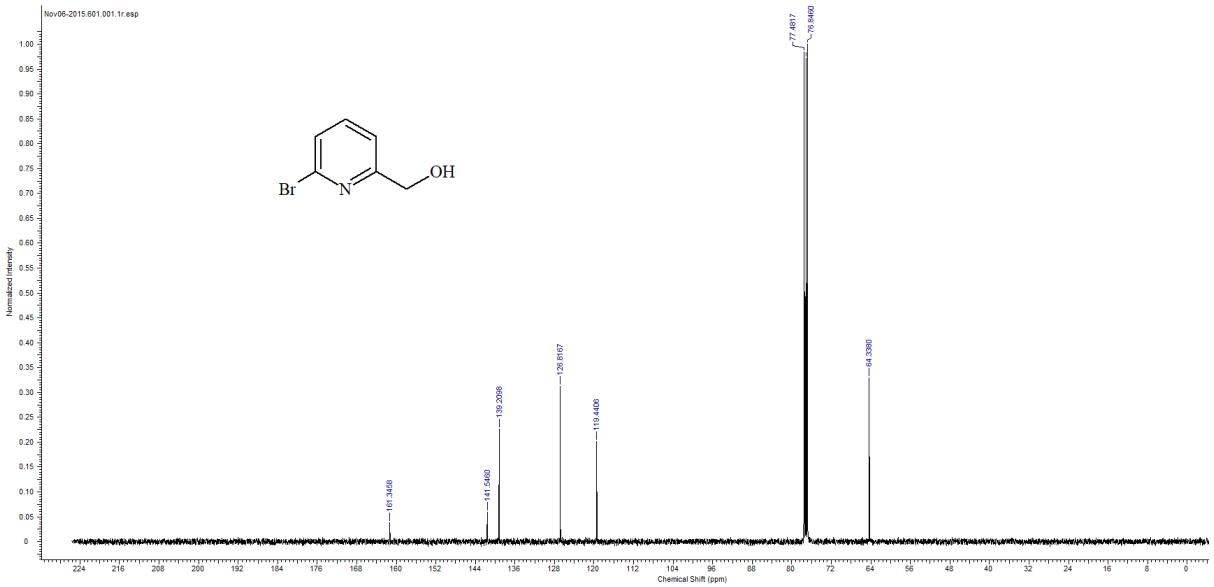
N
OH
Normalized Intensity
Chemical Shift (ppm)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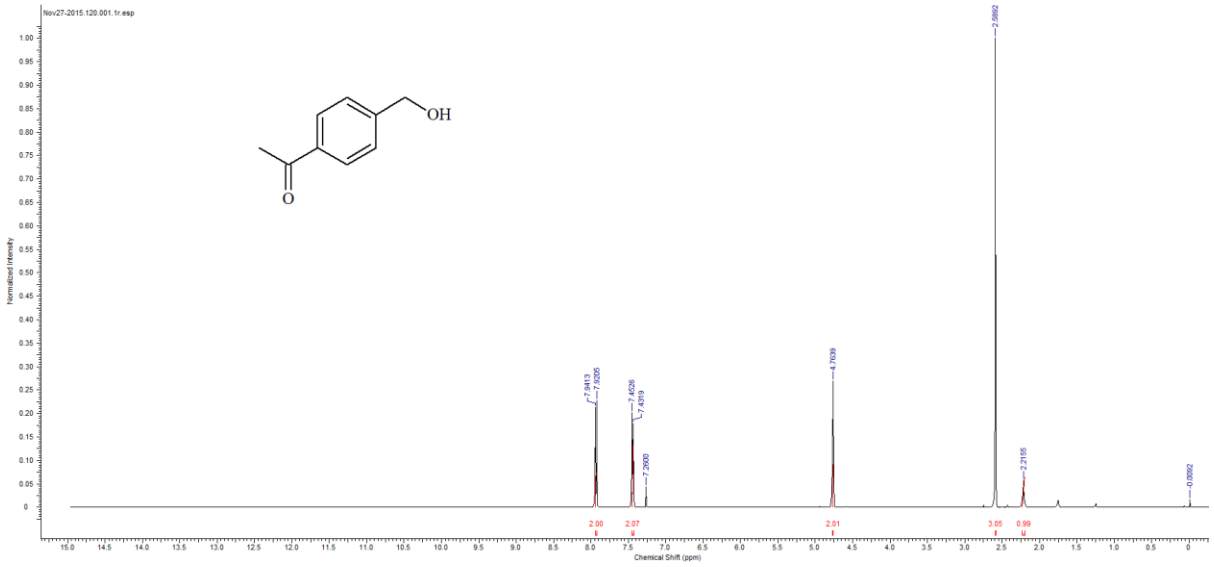
Normalized Intensity
Chemical Shift (ppm)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OH
O
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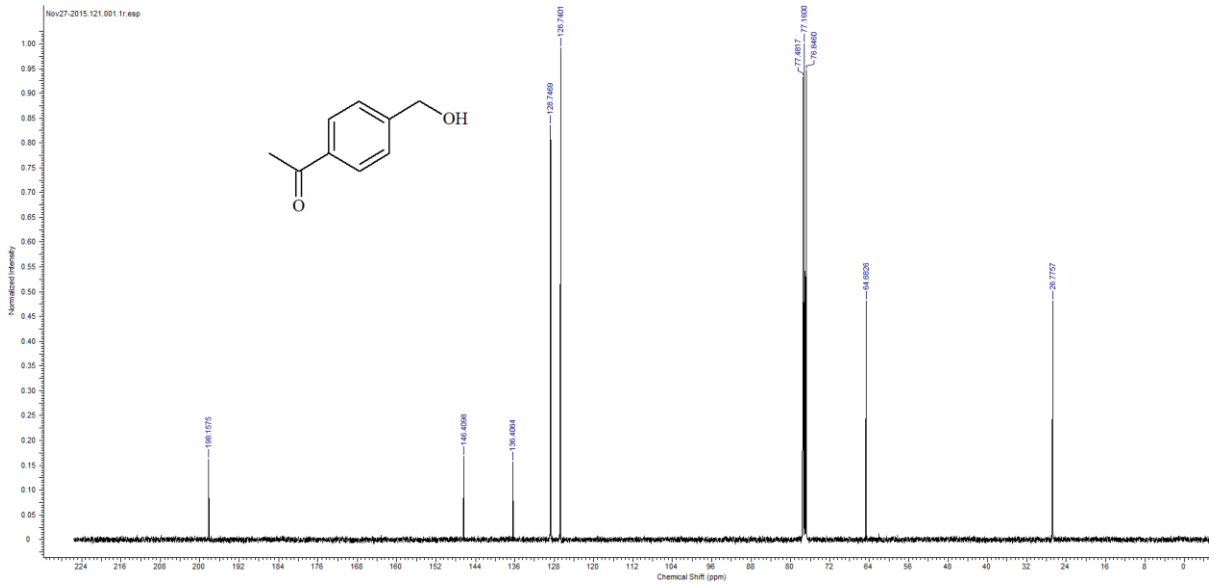
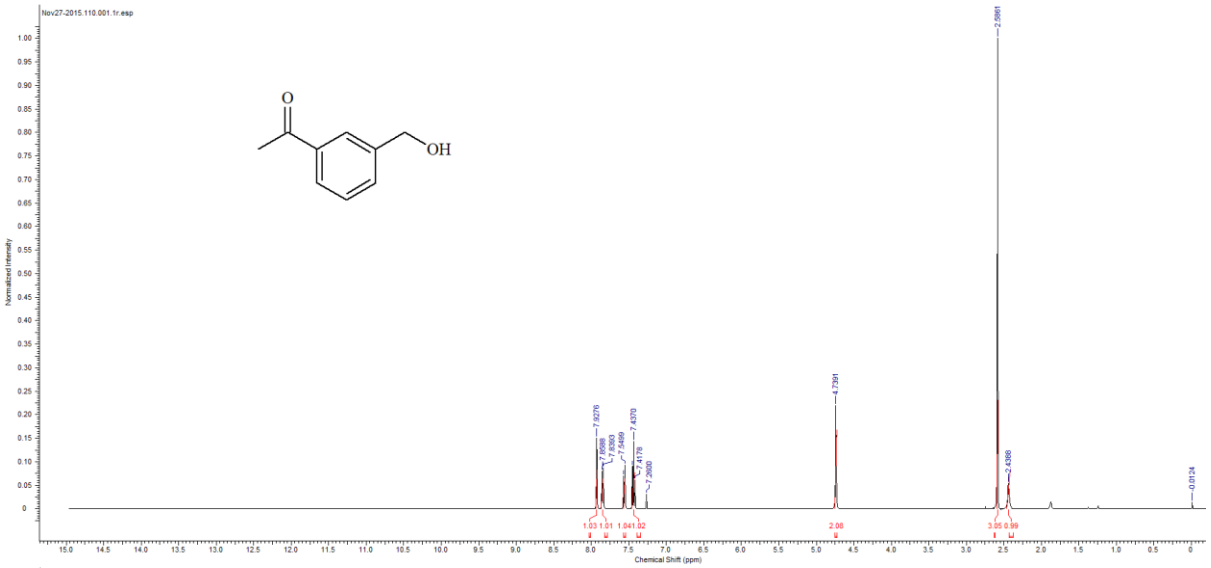
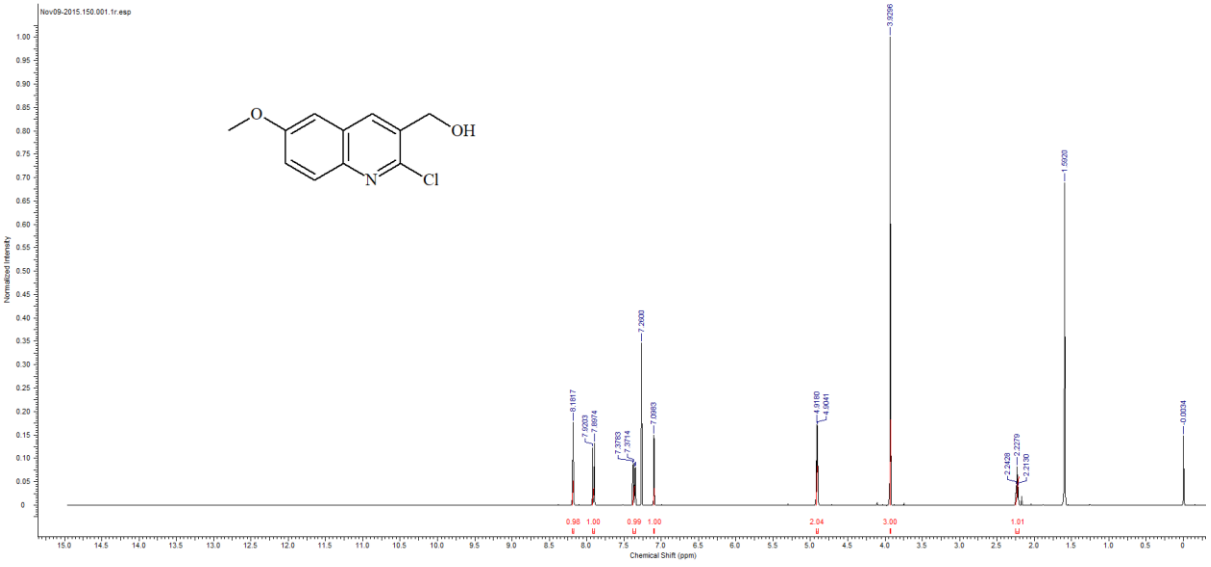
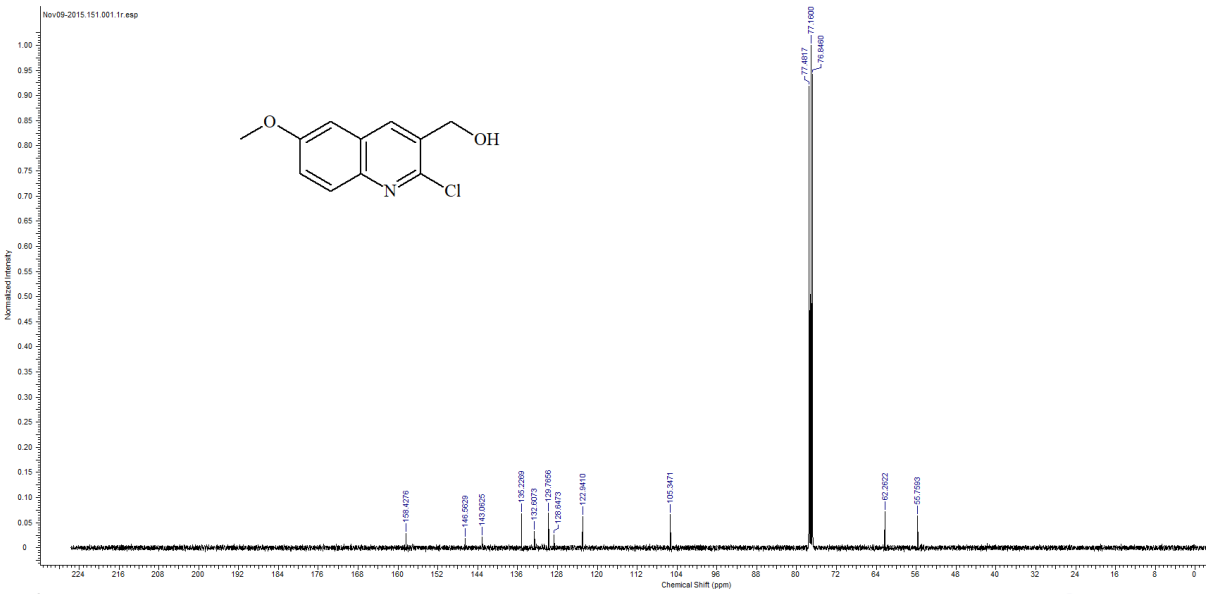
7.4626
7.4519
7.2900
2.2155
0.0892
2.00
2.07
2.01
3.05
0.99
Normalized Intensity
Chemical Shift (ppm)

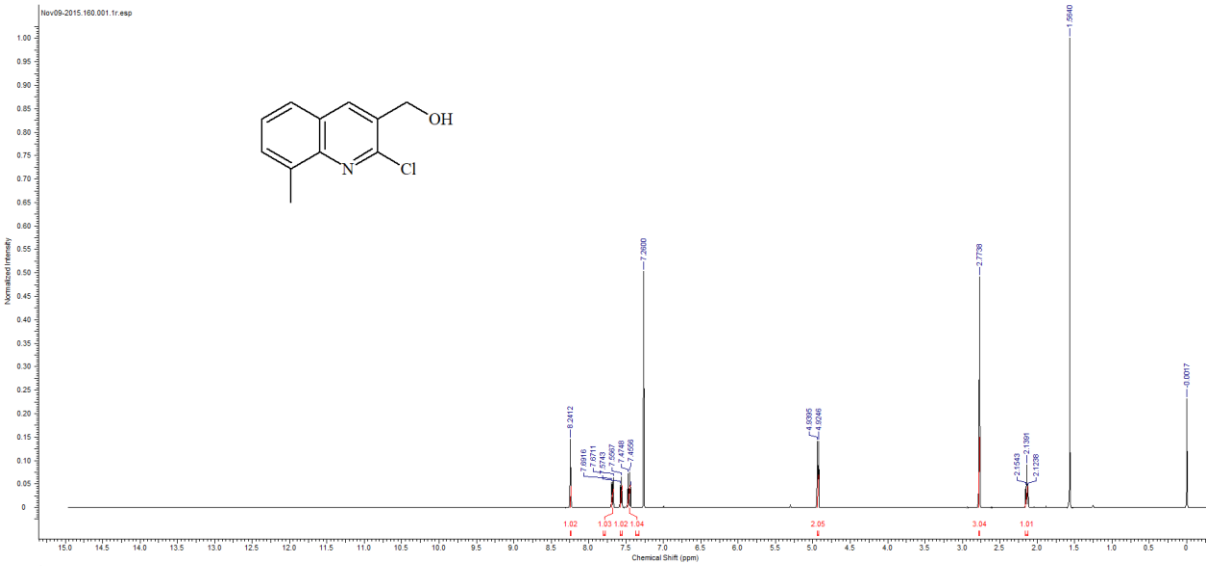

Nov27-2015.121.001.1r.esp
OH
O
126.7401
129.7469
77.4817
77.1600
76.8460
64.6626
26.7707
198.1575
140.4096
136.4004
Normalized Intensity
Chemical Shift (ppm)

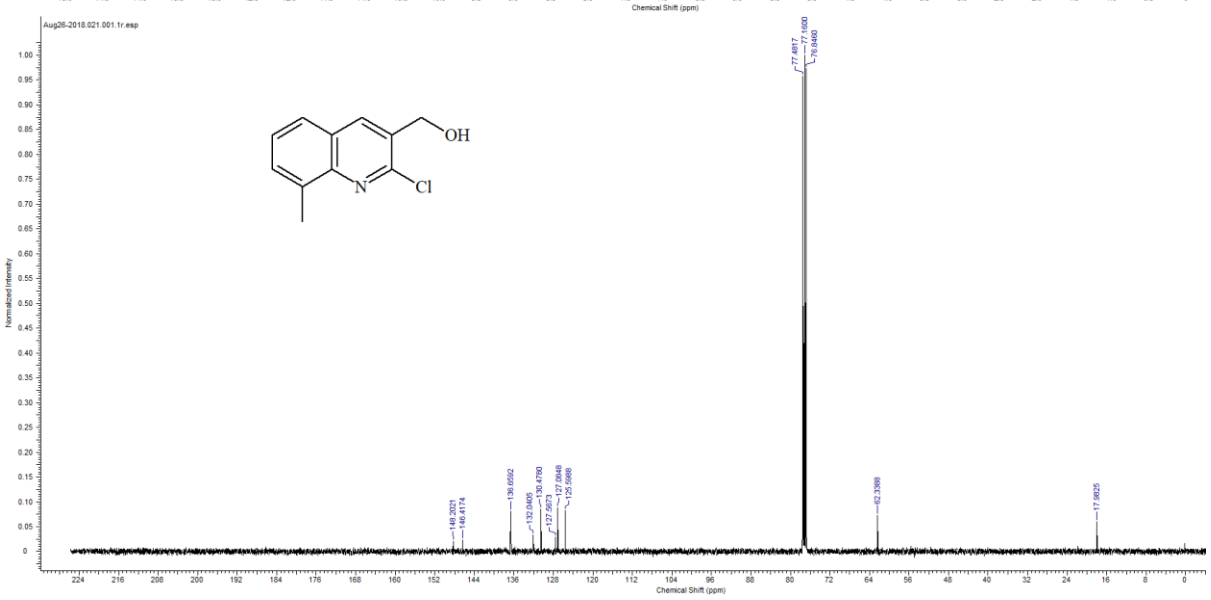

Nov27-2015.110.001.1r.esp
O
OH
Normalized Intensity
Chemical Shift (ppm)

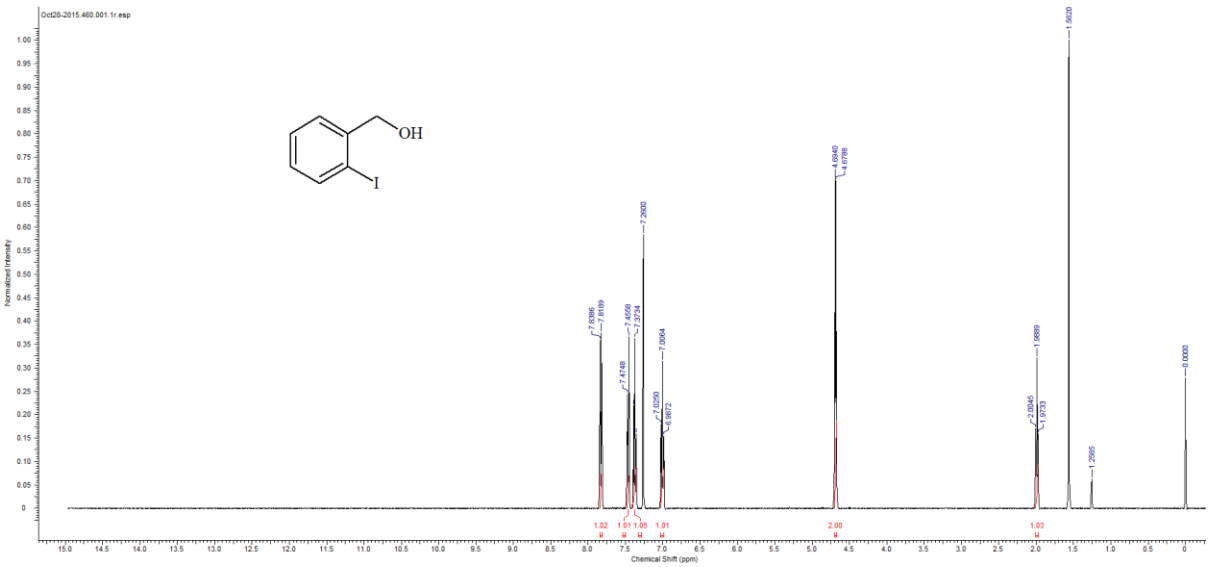

Nov27-2015.111.001.1r.esp
O
OH
Normalized Intensity
Chemical Shift (ppm)

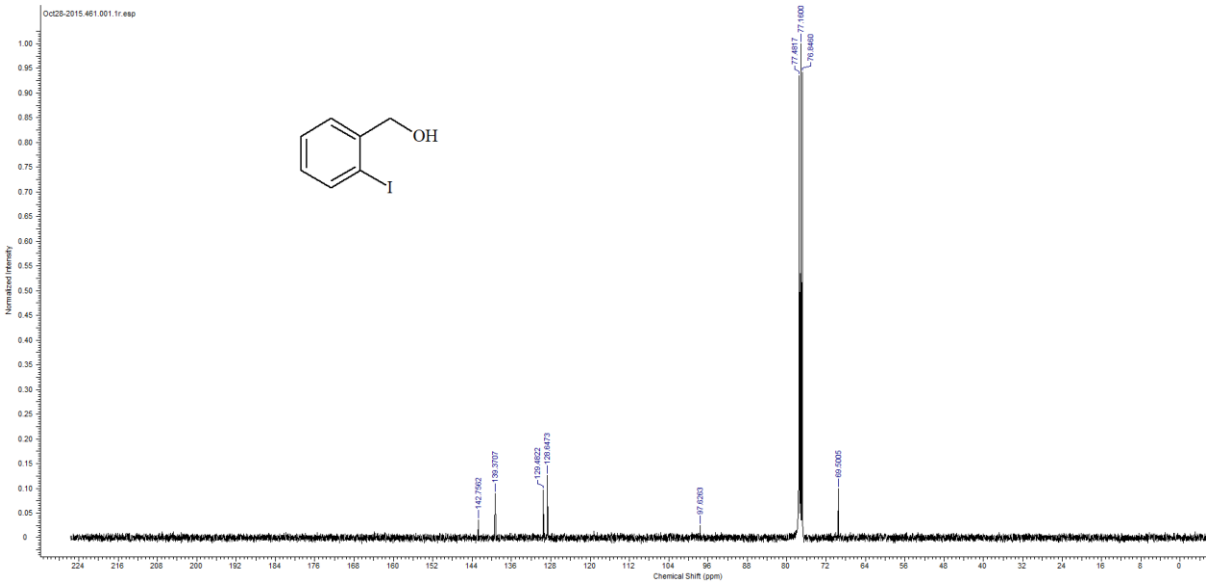

Nov09-2015.150.001.1r.esp
O
OH
N
Cl
Normalized Intensity
Chemical Shift (ppm)

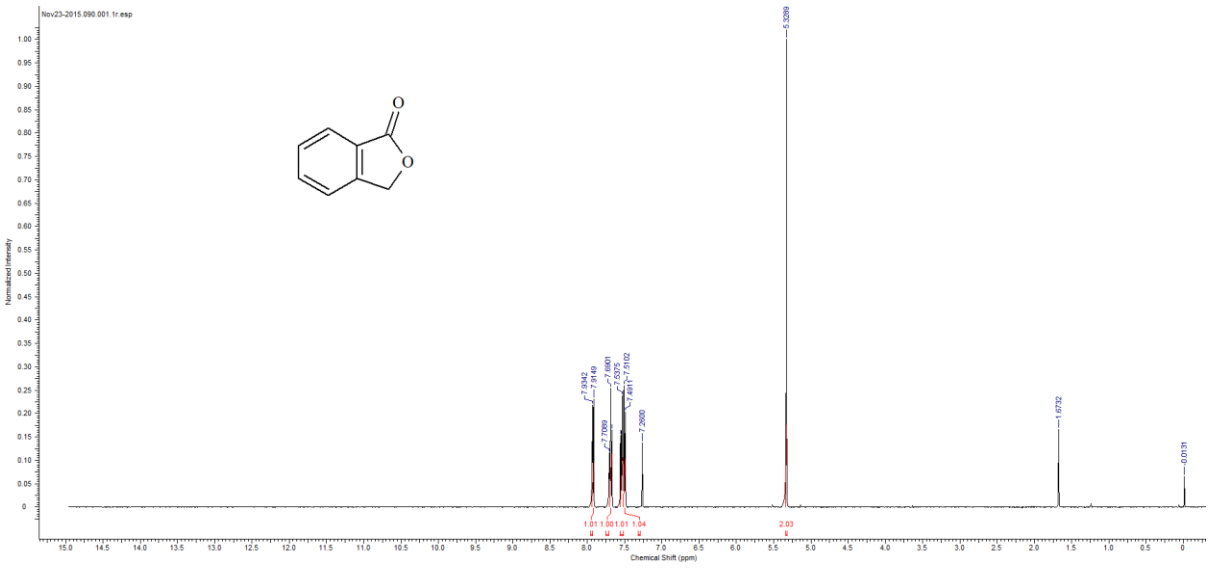

Nov09-2015.151.001.1r.esp
O
OH
N
Cl
Normalized Intensity
Chemical Shift (ppm)

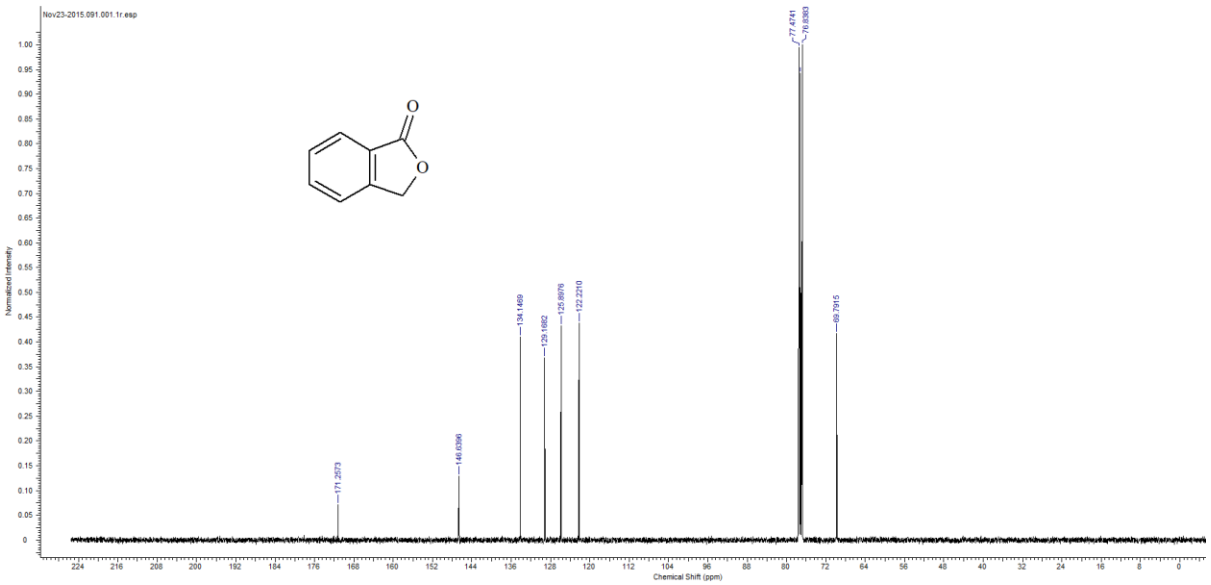

Nov09-2015.160.001.1r.esp
OH
N
Cl
Normalized Intensity
Chemical Shift (ppm)

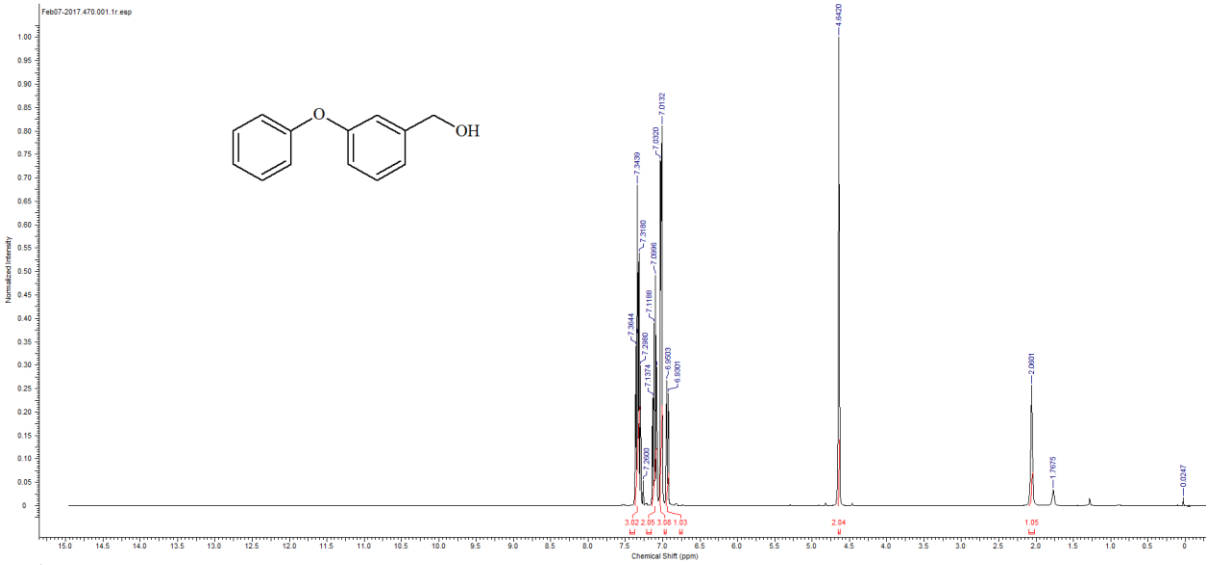

Aug26-2018.021.001.1r.esp
OH
N
Cl
Normalized Intensity
Chemical Shift (ppm)

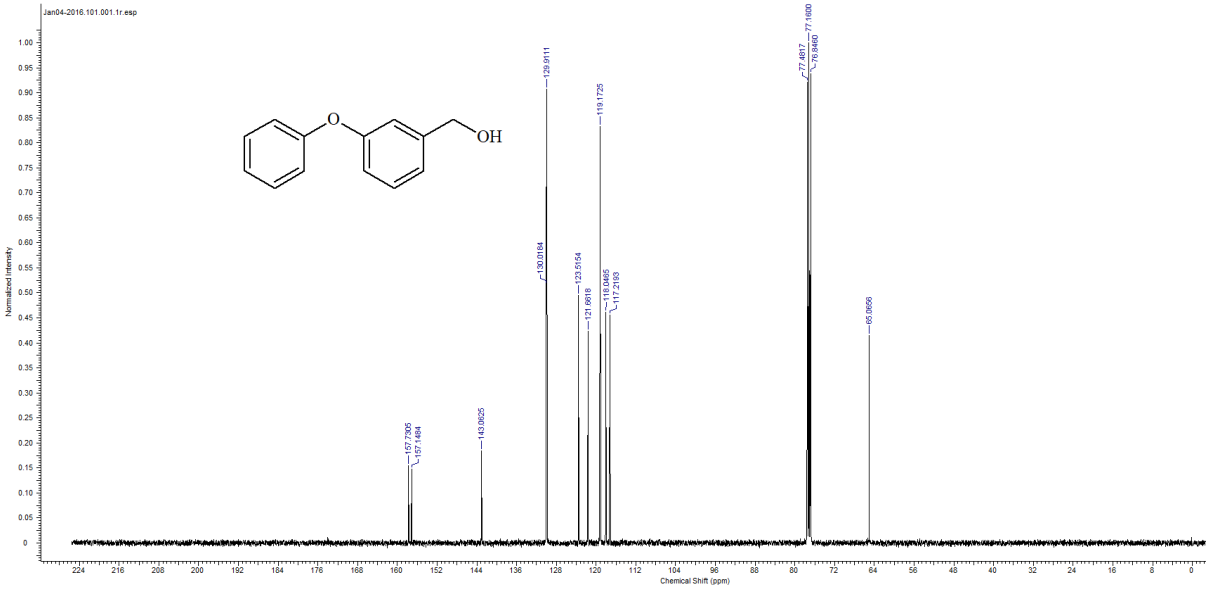

Oct28-2015.460.001.1r.esp
OH
I
Normalized Intensity
Chemical Shift (ppm)

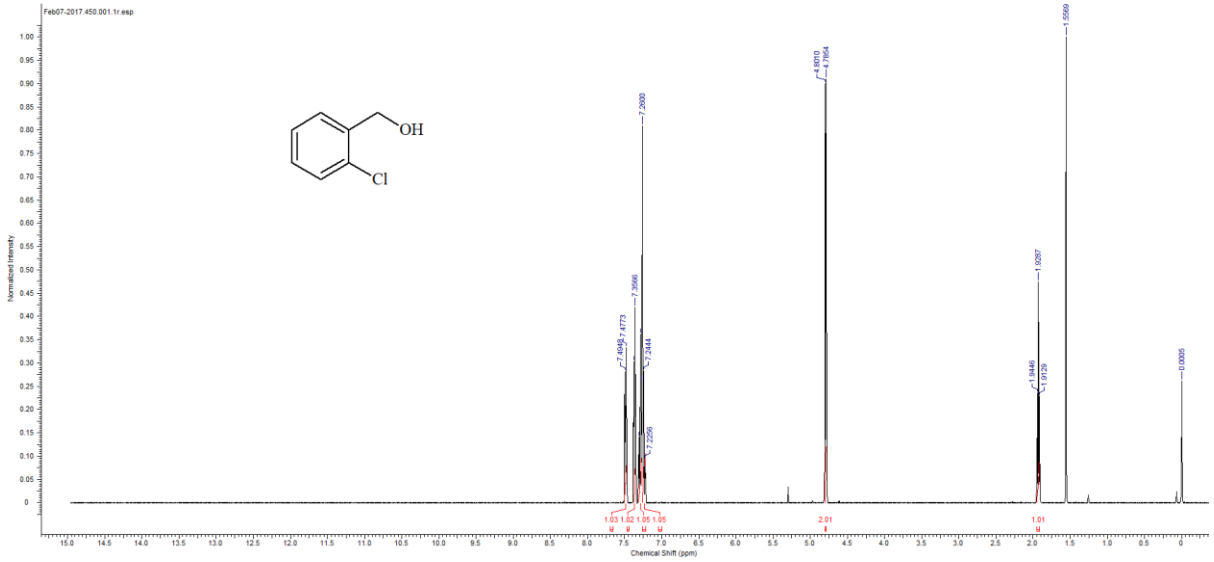

Oct28-2015.461.001.1r.esp
OH
I
Normalized Intensity
Chemical Shift (ppm)

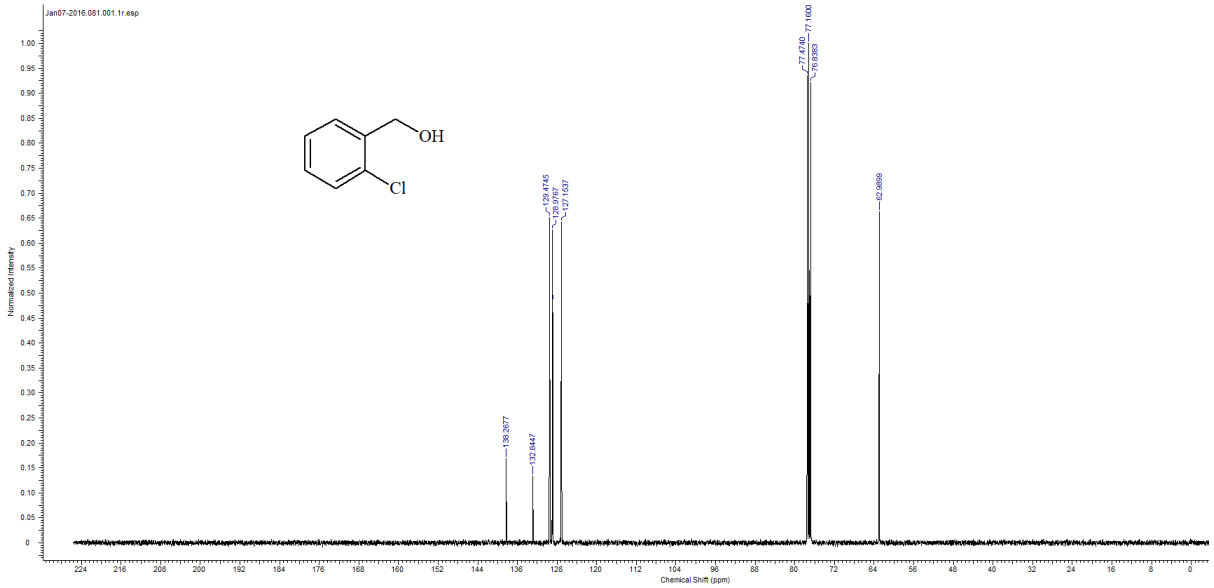

Nov23-2015.090.001.1r.esp
O
O
Normalized Intensity
Chemical Shift (ppm)

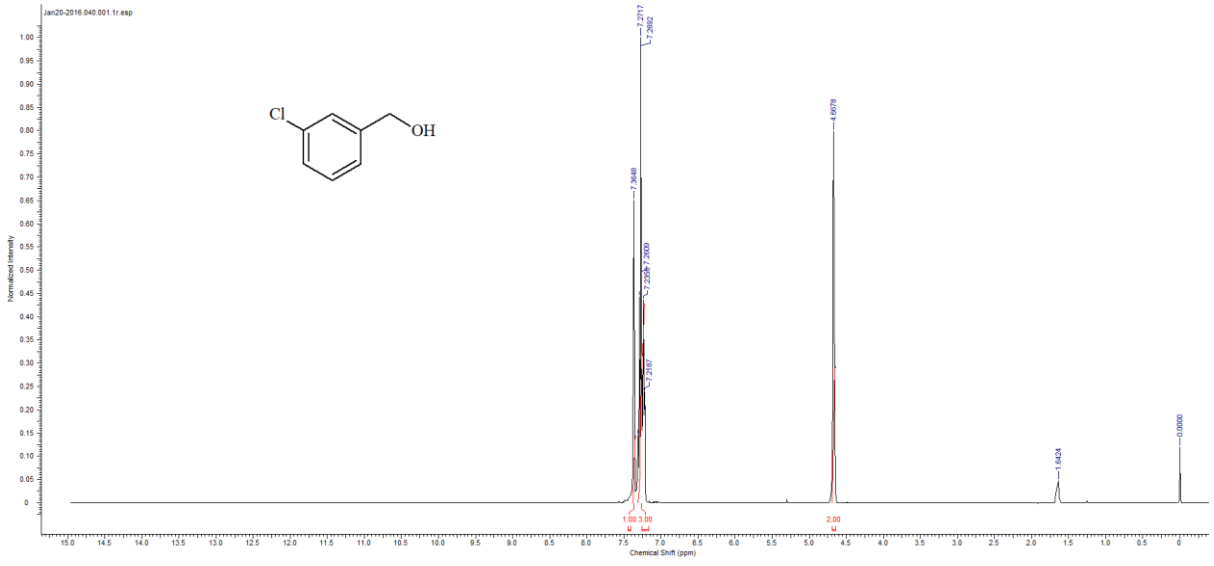

Nov23-2015.091.001.1r.esp
O
O
77.4741
76.8363
134.1469
129.1662
125.8976
123.2210
89.7915
171.2673
146.6396
Normalized Intensity
Chemical Shift (ppm)

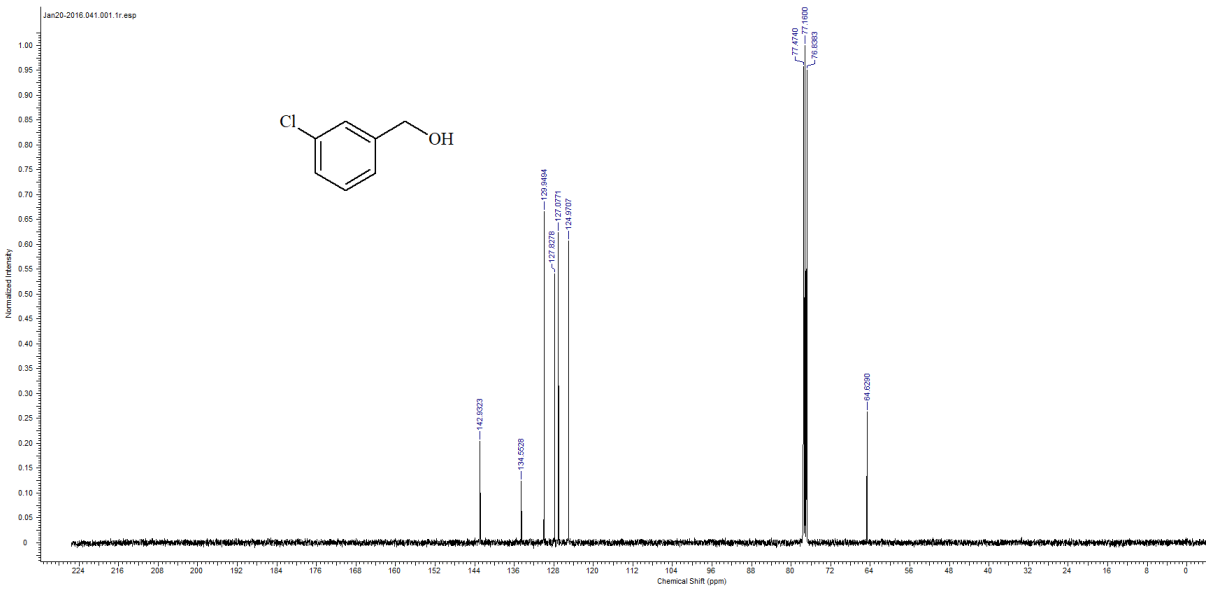

Feb07-2017.470.001.1r.esp
O
OH
4.6420
7.0132
7.0030
7.3439
7.3180
7.0999
7.1188
7.3644
7.2680
7.1374
6.9503
6.8061
2.0601
1.7675
0.0247
3.02 2.05 3.08 1.03
2.04
1.05
Normalized Intensity
Chemical Shift (ppm)

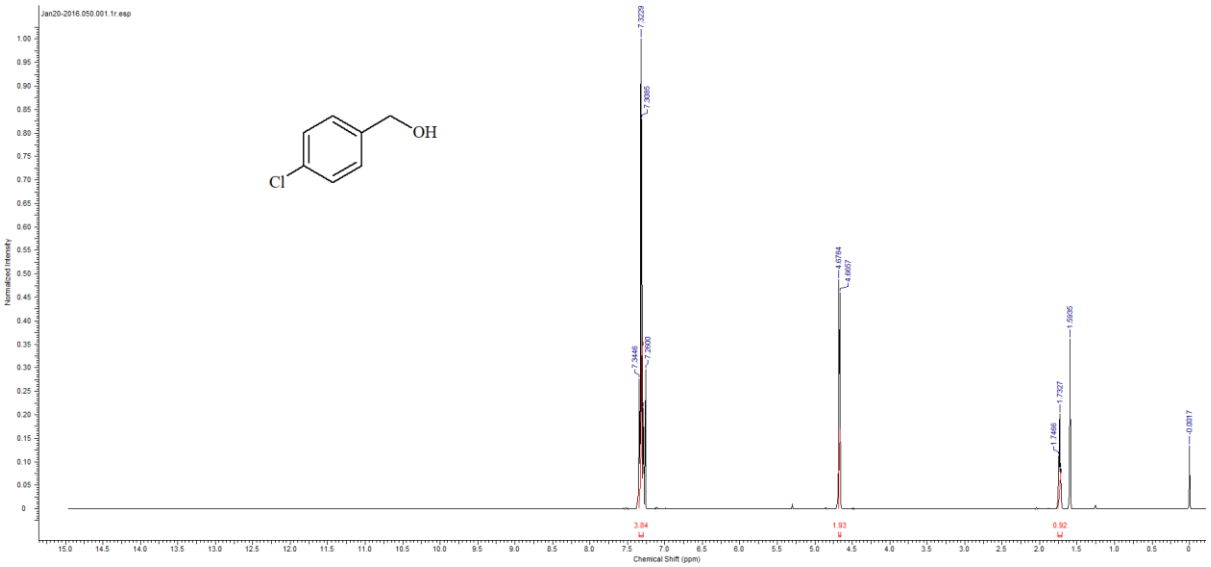

Jan04-2016.101.001.1r.esp
O
OH
129.9111
119.1725
77.4817
77.1600
76.8460
130.0184
123.5154
121.6618
118.0465
117.2163
85.0659
157.7305
157.1484
143.0625
Normalized Intensity
Chemical Shift (ppm)

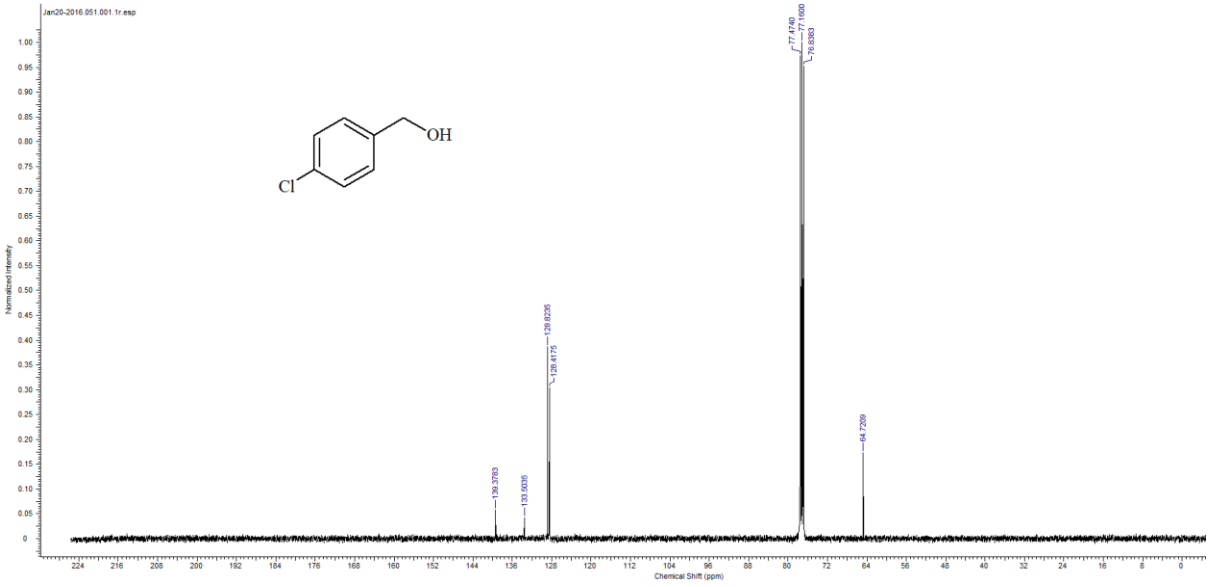

Feb07-2017.450.001.1r.esp
OH
Cl
Normalized Intensity
Chemical Shift (ppm)

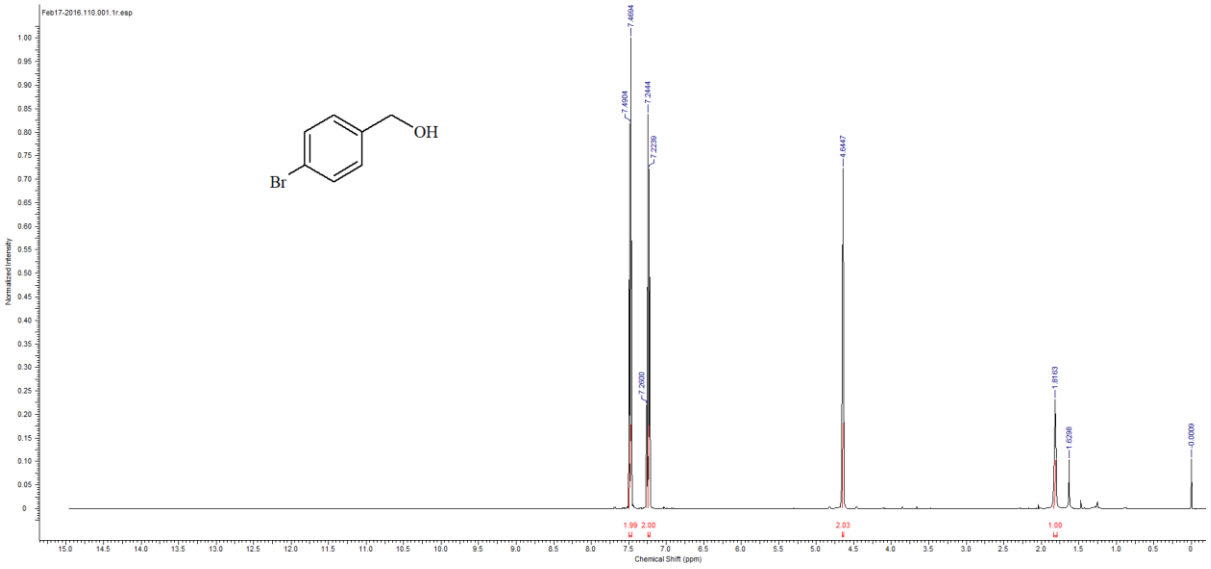

Jan07-2016.081.001.1r.esp
OH
Cl
Normalized Intensity
Chemical Shift (ppm)

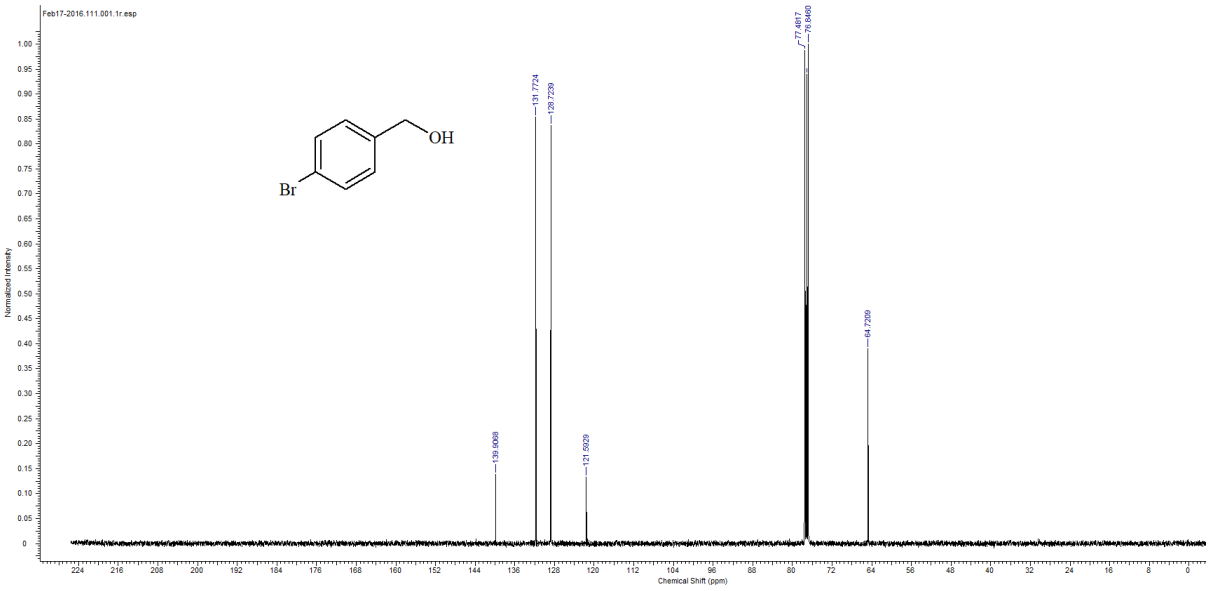

Jan20-2016.040.001.1r.esp
Cl
OH
Normalized Intensity
Chemical Shift (ppm)

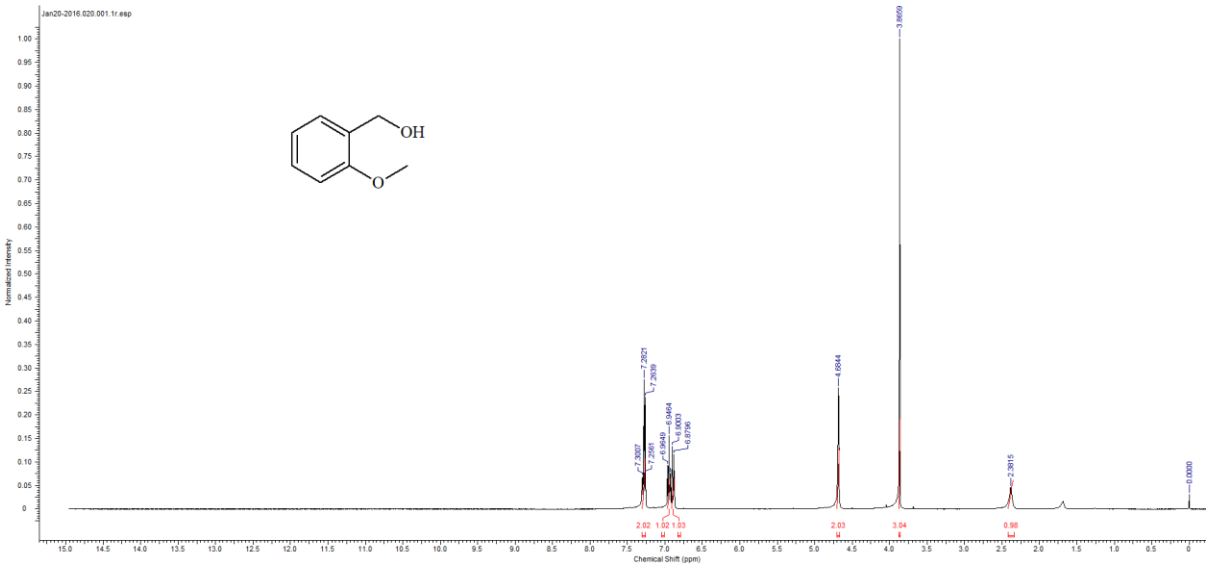

Jan20-2016.041.001.1r.esp
Cl
OH
77.4740
77.1600
76.8383
129.9464
127.6278
127.0771
124.9707
142.6323
134.5528
64.6290
Normalized Intensity
Chemical Shift (ppm)

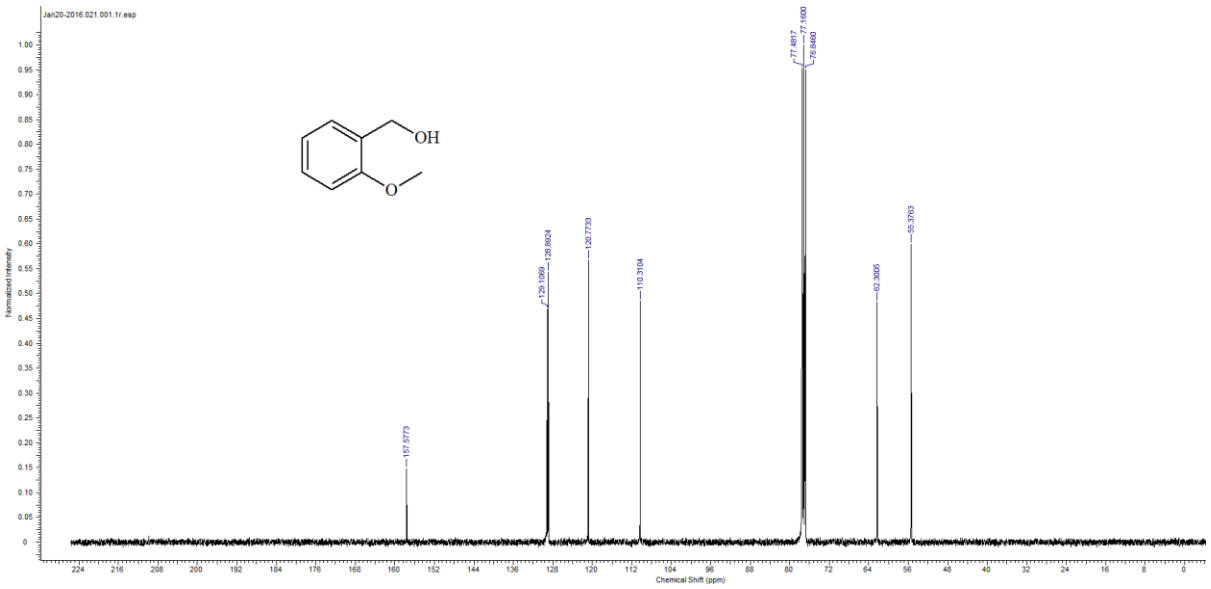

Jan20-2016.050.001.1r.esp
OH
Cl
7.3229
7.3085
4.6784
4.6657
7.3446
7.2980
1.5935
1.7327
1.7466
0.0817
3.84
1.93
0.92
Normalized Intensity
Chemical Shift (ppm)

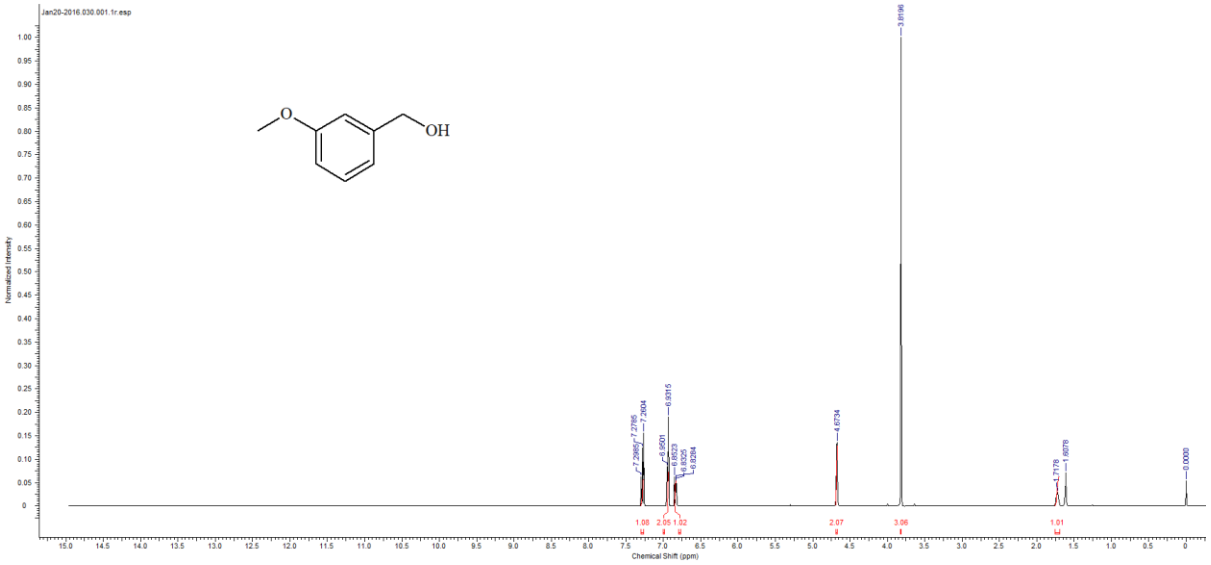

Jan20-2016.051.001.1r.esp
OH
Cl
77.4740
77.1600
76.8383
128.8235
128.4175
139.3763
133.8035
64.7209
Normalized Intensity
Chemical Shift (ppm)

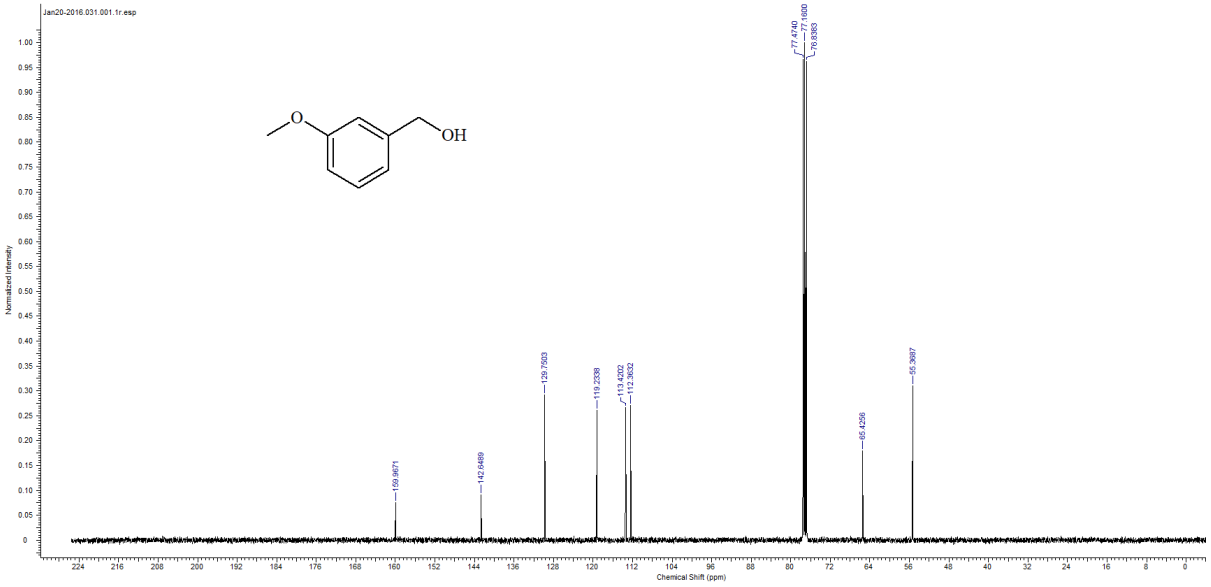

Feb17-2016.110.001.1r.esp
OH
Br
Normalized Intensity
Chemical Shift (ppm)

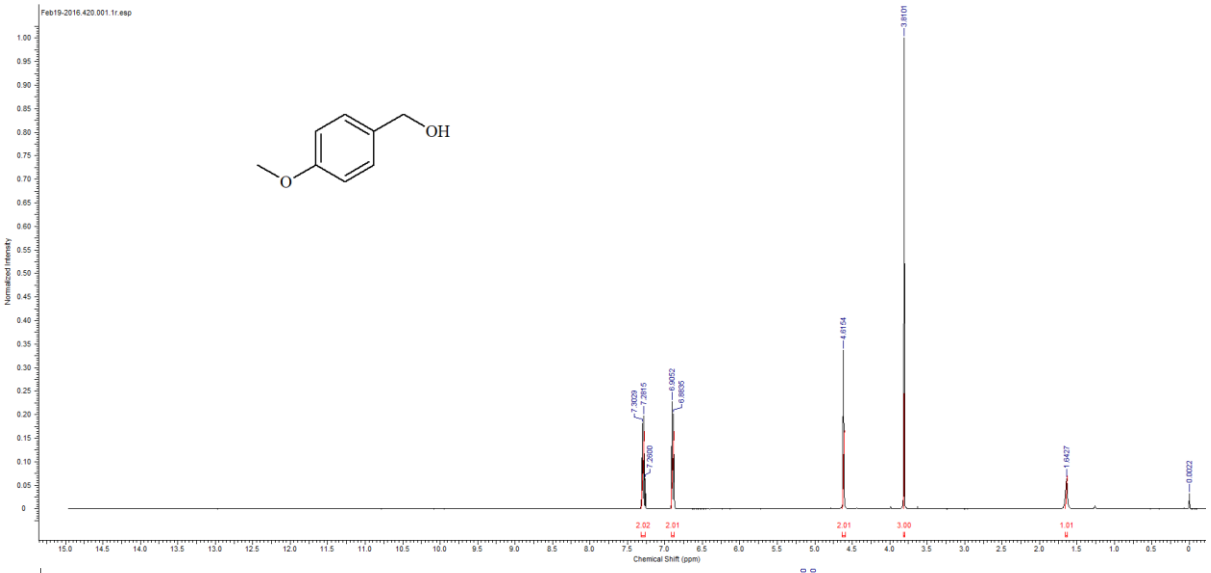

Feb17-2016.111.001.1r.esp
OH
Br
Normalized Intensity
Chemical Shift (ppm)


Jan20-2016.020.001.1r.esp
OH
O
Normalized Intensity
Chemical Shift (ppm)

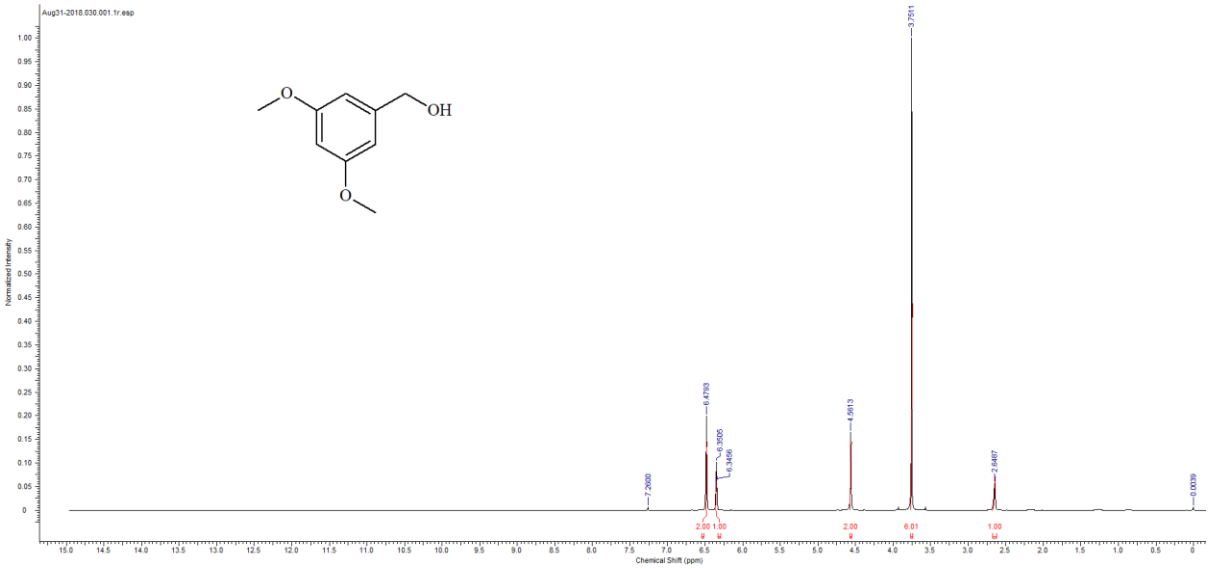

Jan20-2016.021.001.1r.esp
OH
O
157.5773
129.1069
128.8924
120.7733
110.3104
77.4817
77.1600
76.8460
62.3005
55.3763
Normalized Intensity
Chemical Shift (ppm)

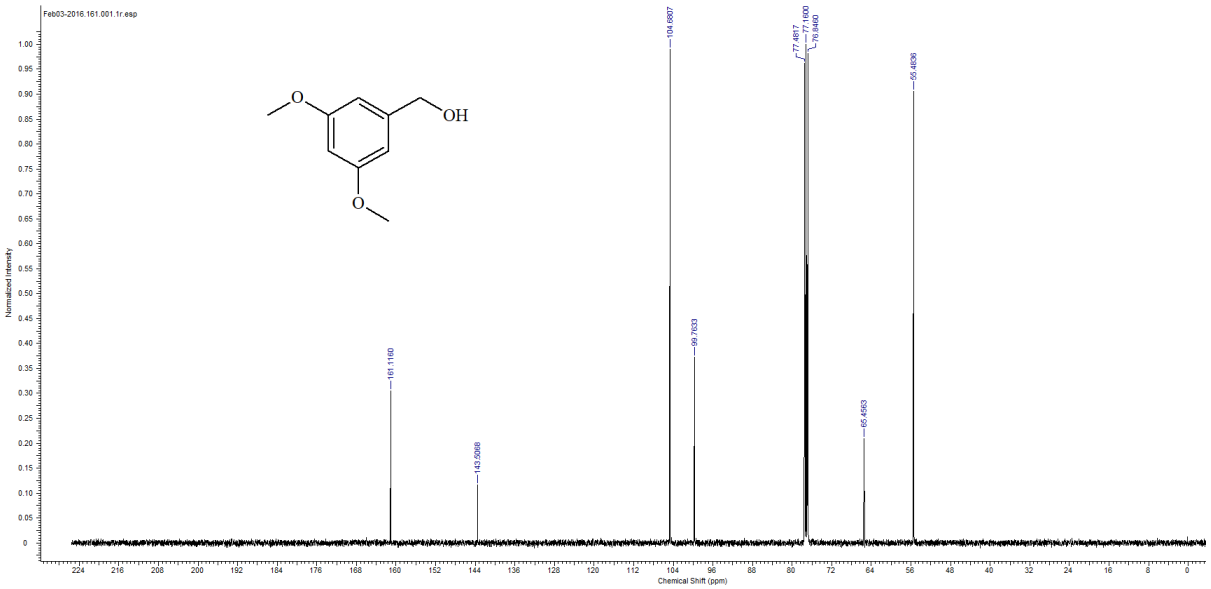

Jan20-2016.030.001.1r.esp
O
OH
7.2995
7.2785
7.2604
6.9501
6.9315
6.8523
6.8305
6.8284
4.6734
3.8196
1.7178
1.6078
0.0000
1.08
2.05
1.02
2.07
3.06
1.01
Normalized Intensity
Chemical Shift (ppm)

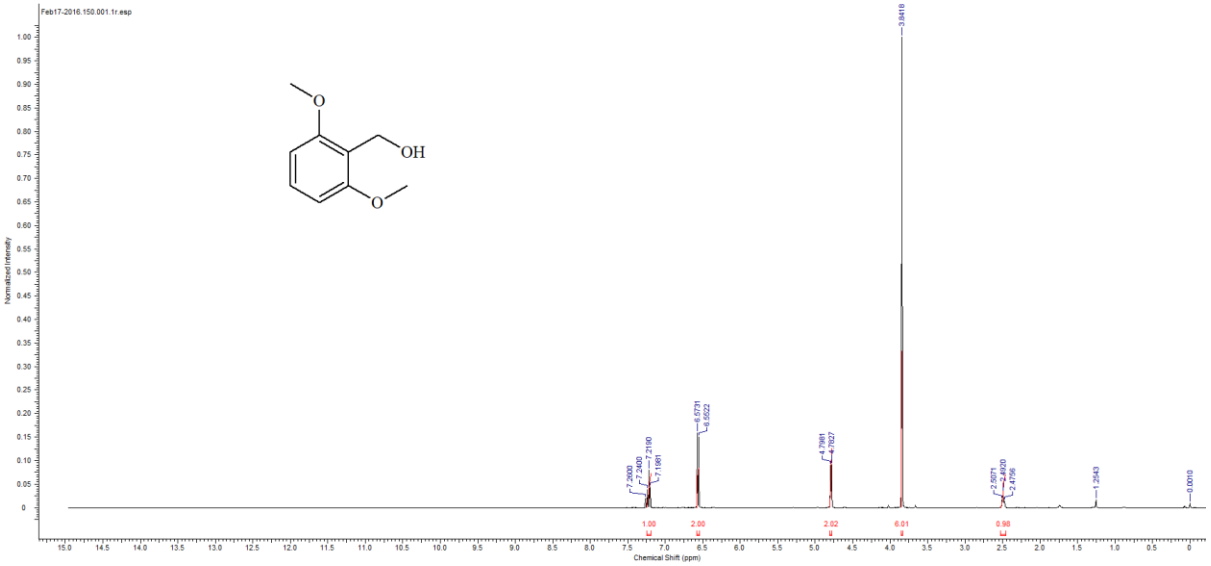

Jan20-2016.031.001.1r.esp
O
OH
159.9871
142.6469
129.7503
119.2338
113.4202
112.3632
77.4740
77.1600
76.8383
65.4256
55.3697
Normalized Intensity
Chemical Shift (ppm)


Feb19-2016.420.001.1r.esp
OH
O
Normalized Intensity
Chemical Shift (ppm)

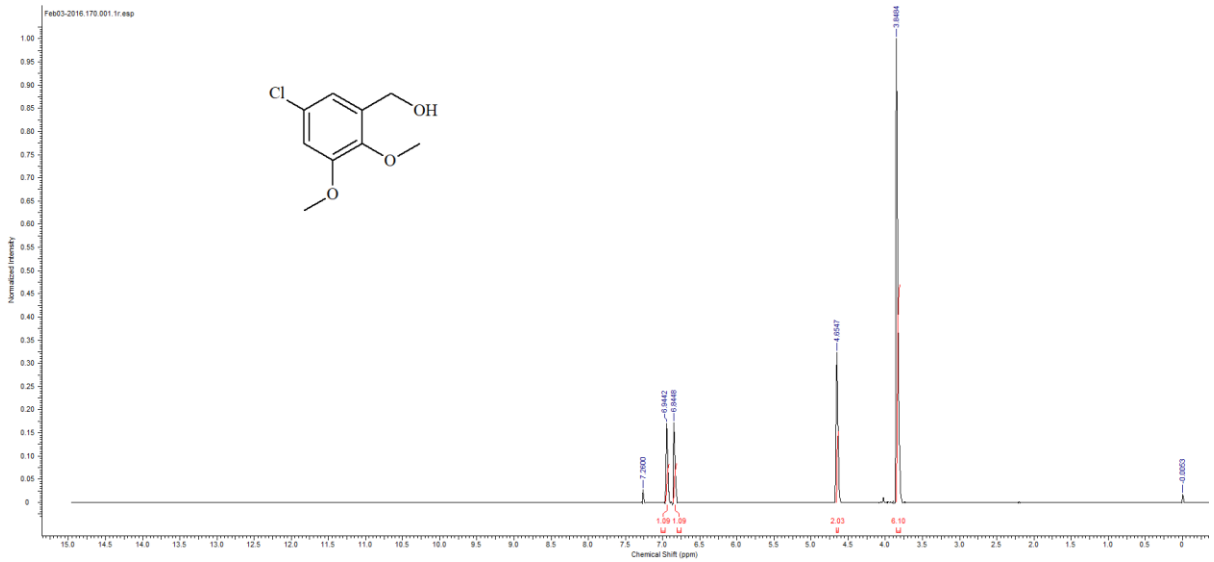

Feb19-2016.421.001.1r.esp
OH
O
Normalized Intensity
Chemical Shift (ppm)

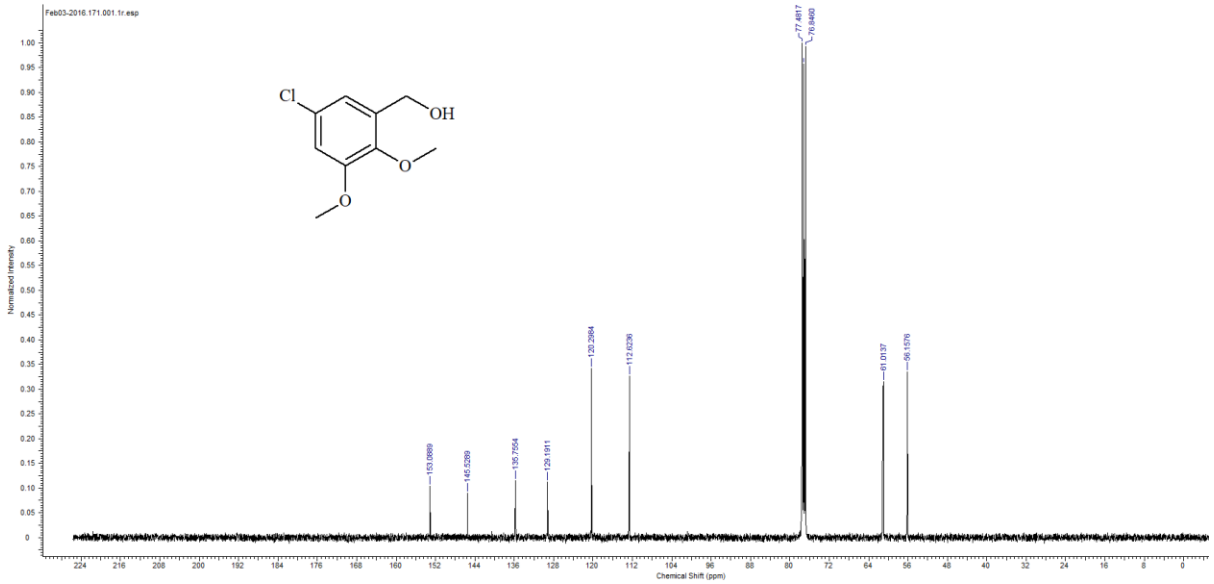

Aug31-2018.030.001.1r.esp
OH
O
O
Normalized Intensity
Chemical Shift (ppm)

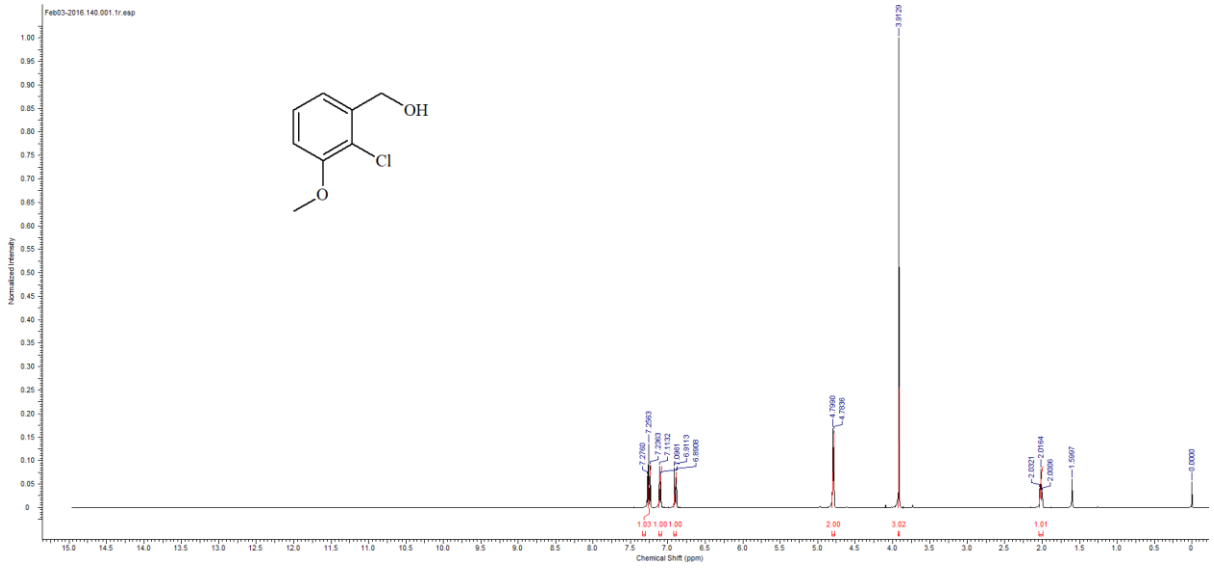

Feb03-2016.161.001.1r.esp
O
OH
O
104.6807
77.4817
77.1600
76.8460
55.4839
99.7633
161.1160
143.0968
65.4563
Normalized Intensity
Chemical Shift (ppm)

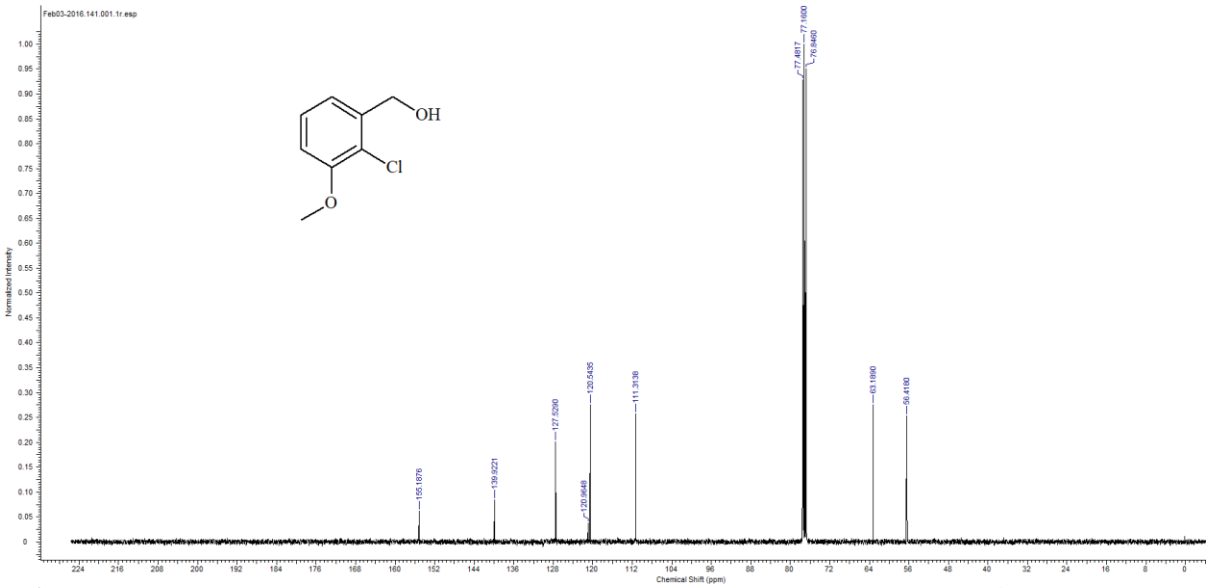

Feb17-2016.150.001.1r.esp
O
OH
O
3.8418
7.2600
7.2405
7.1961
7.7190
6.5731
6.5522
4.7981
4.7827
2.5971
2.4920
2.4766
1.2543
0.0010
1.00
2.00
2.02
6.01
0.98
Normalized Intensity
Chemical Shift (ppm)

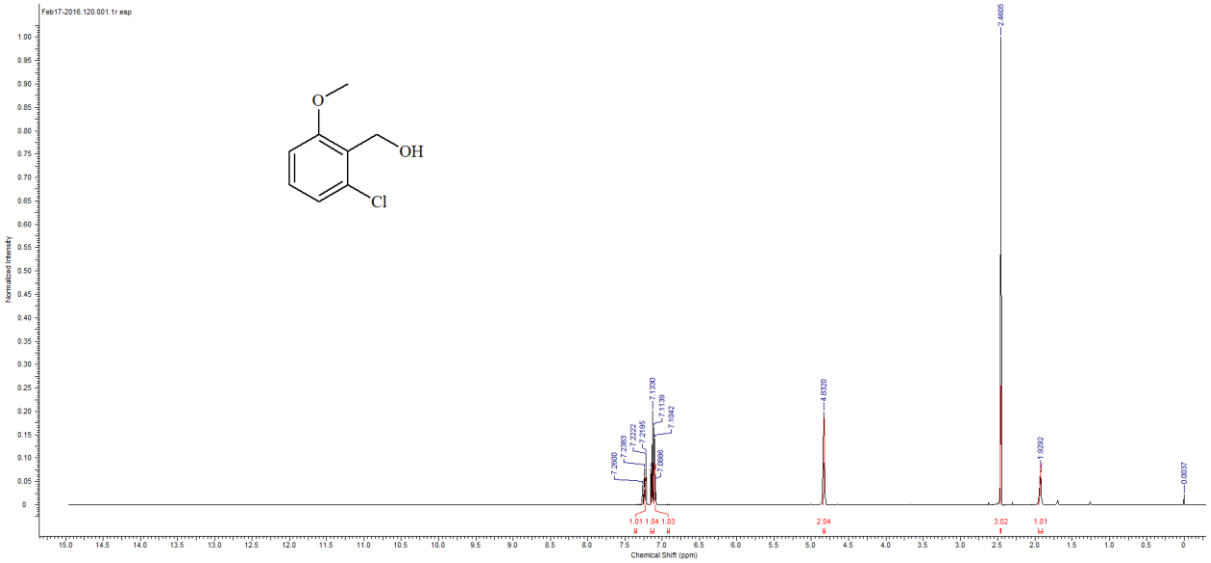

Feb17-2016.151.001.1r.esp
O
OH
O
103.9454
55.8689
77.4817
77.1600
76.8460
129.2601
54.5478
158.5348
117.1657
29.8165
Normalized Intensity
Chemical Shift (ppm)

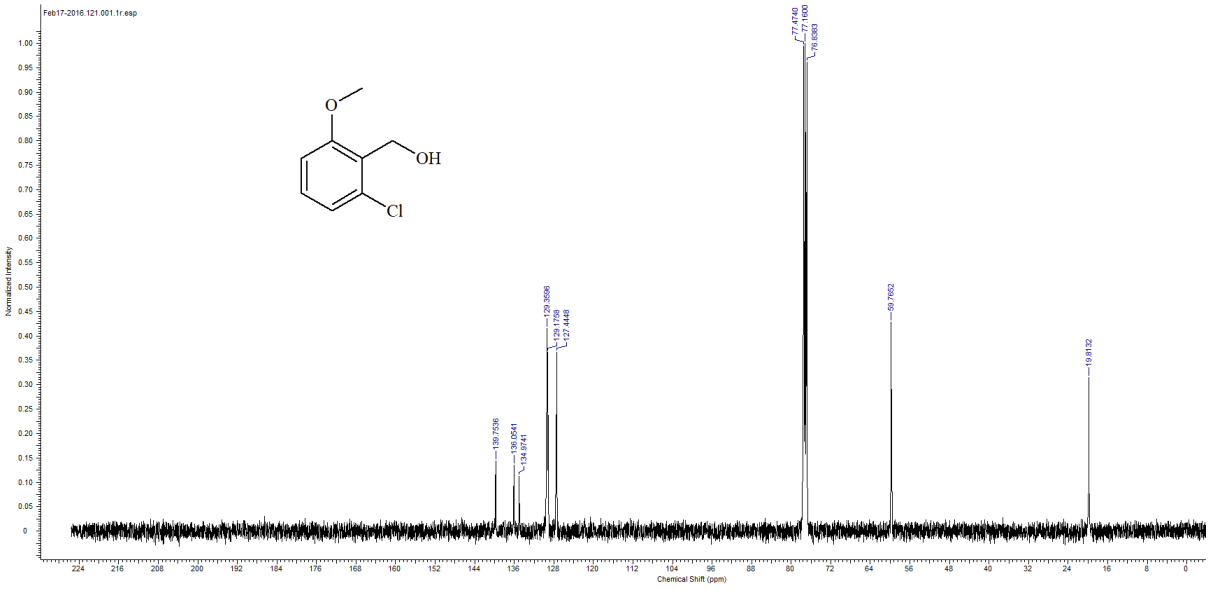

Feb03-2016.170.001.1r.esp
Cl
OH
O
O
Normalized Intensity
Chemical Shift (ppm)
3.9484
4.6547
7.2600
6.9442
6.9448
0.0053
1.09 1.09
2.03
6.10

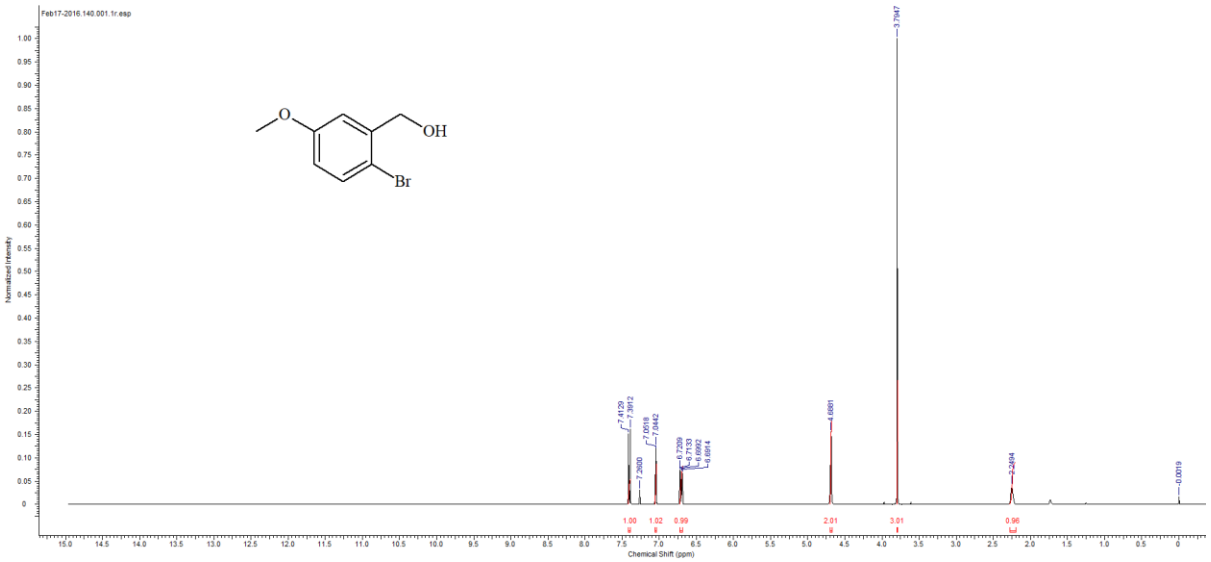

Feb03-2016.171.001.1r.esp
Cl
OH
O
O
Normalized Intensity
Chemical Shift (ppm)
77.4817
76.9460
153.0069
145.5289
135.7554
129.1911
120.2984
112.6239
61.0157
56.1570


Feb03-2016.140.001.1r.esp
OH
Cl
O
Normalized Intensity
Chemical Shift (ppm)
3.9129
7.2769
7.2953
7.3293
7.3432
7.0661
6.9113
6.8908
4.7990
4.7836
2.0321
2.0164
2.0006
1.5907
0.0000
1.03 1.00 1.00 1.00
2.00
3.02
1.01

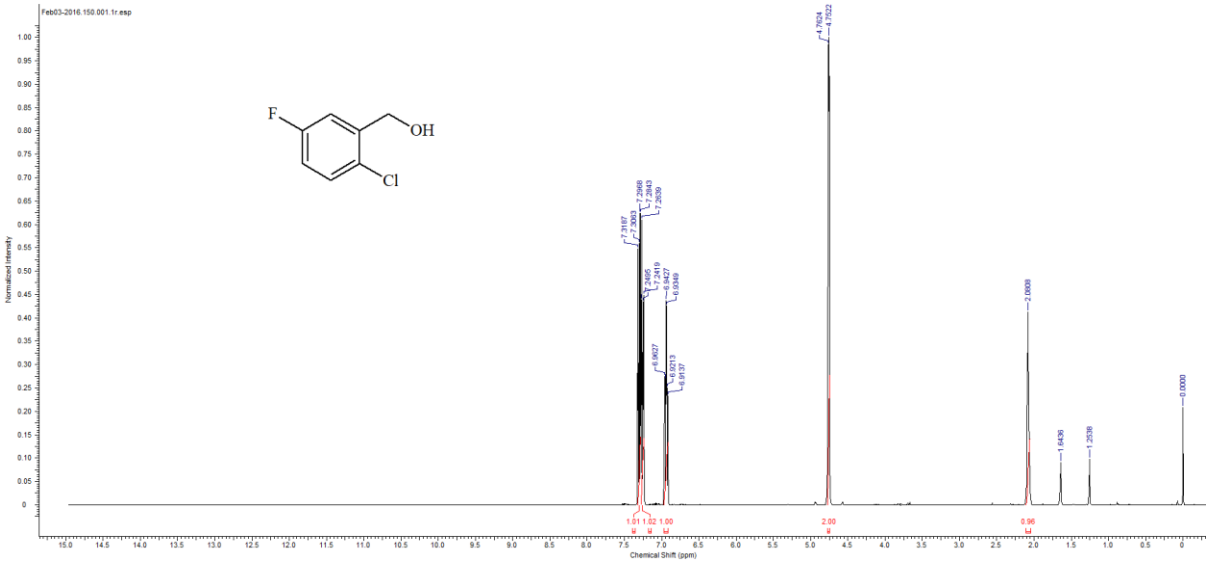

Feb03-2016.141.001.1r.esp
OH
Cl
O
Normalized Intensity
Chemical Shift (ppm)

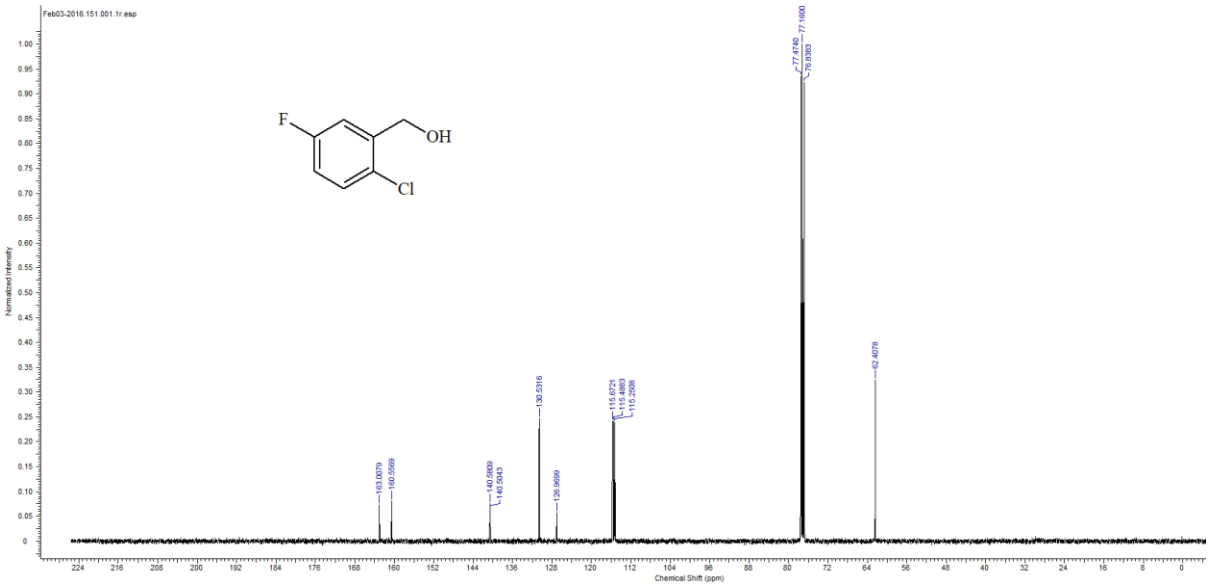

Feb17-2016.120.001.1r.esp
O
OH
Cl
Normalized Intensity
Chemical Shift (ppm)

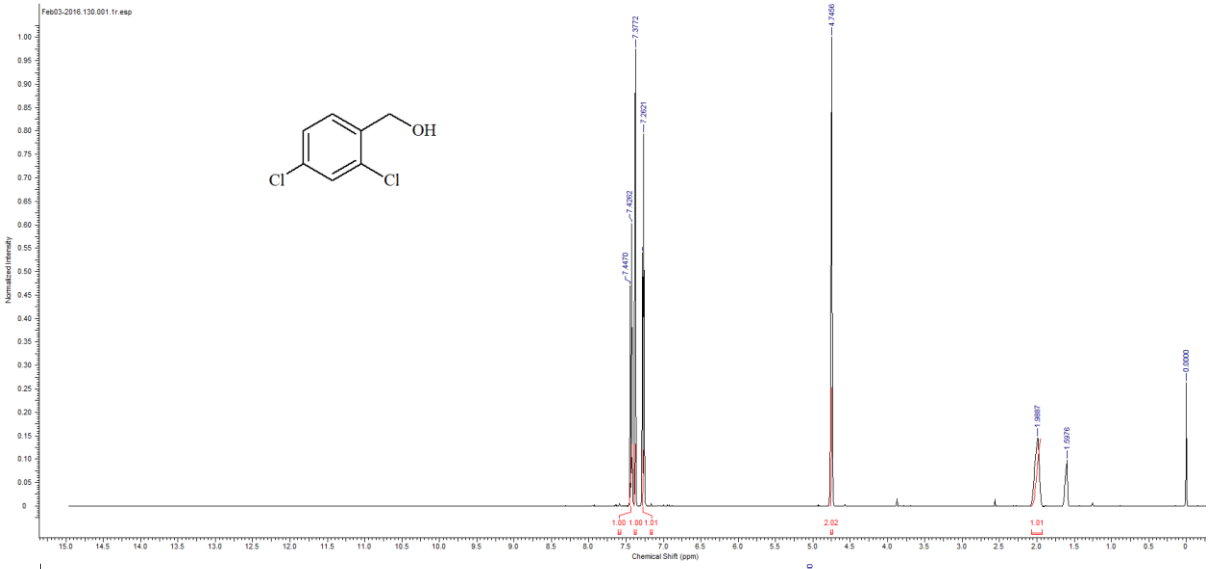

Feb17-2016.121.001.1r.esp
O
OH
Cl
Normalized Intensity
Chemical Shift (ppm)

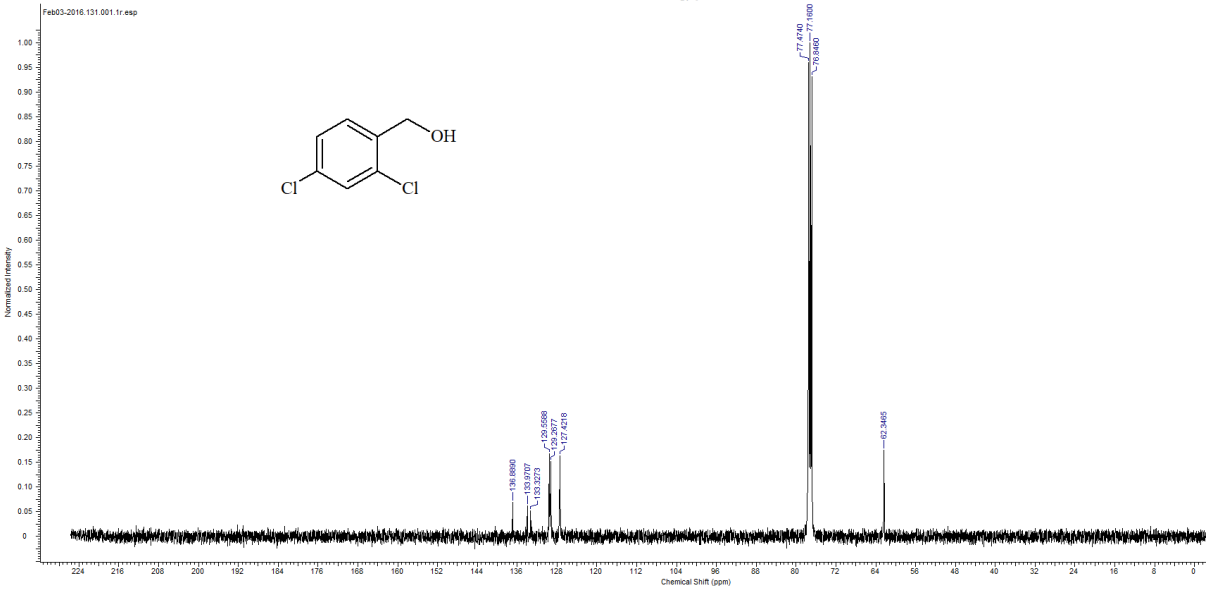

Feb17-2016.140.001.1r.esp
O
OH
Br
Normalized Intensity
Chemical Shift (ppm)

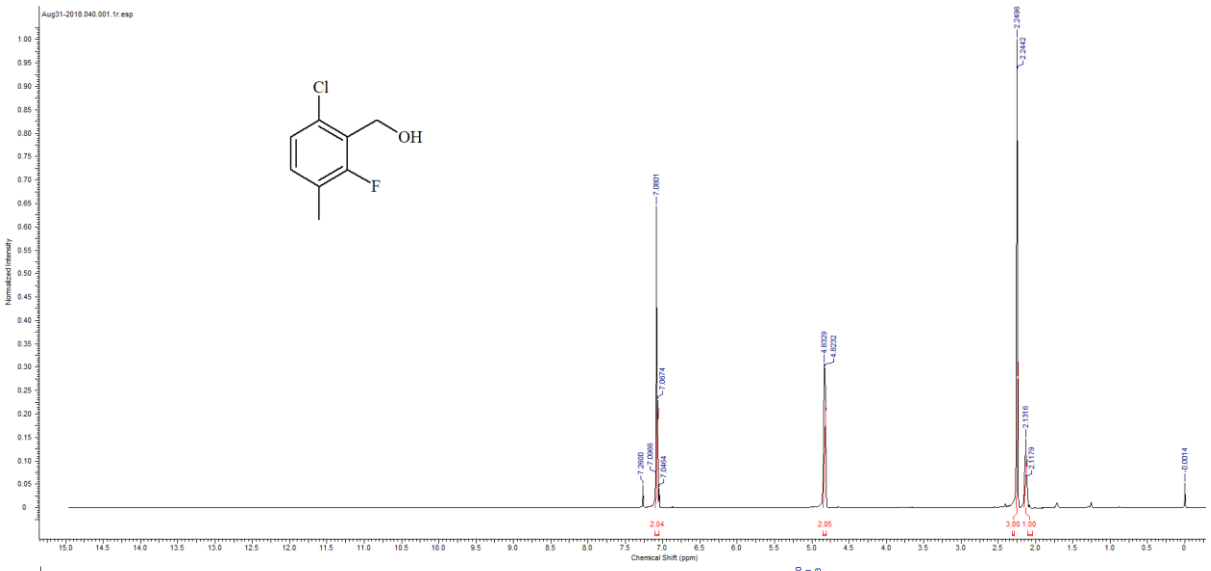

Feb17-2016.141.001.1r.esp
O
OH
Br
Normalized Intensity
Chemical Shift (ppm)

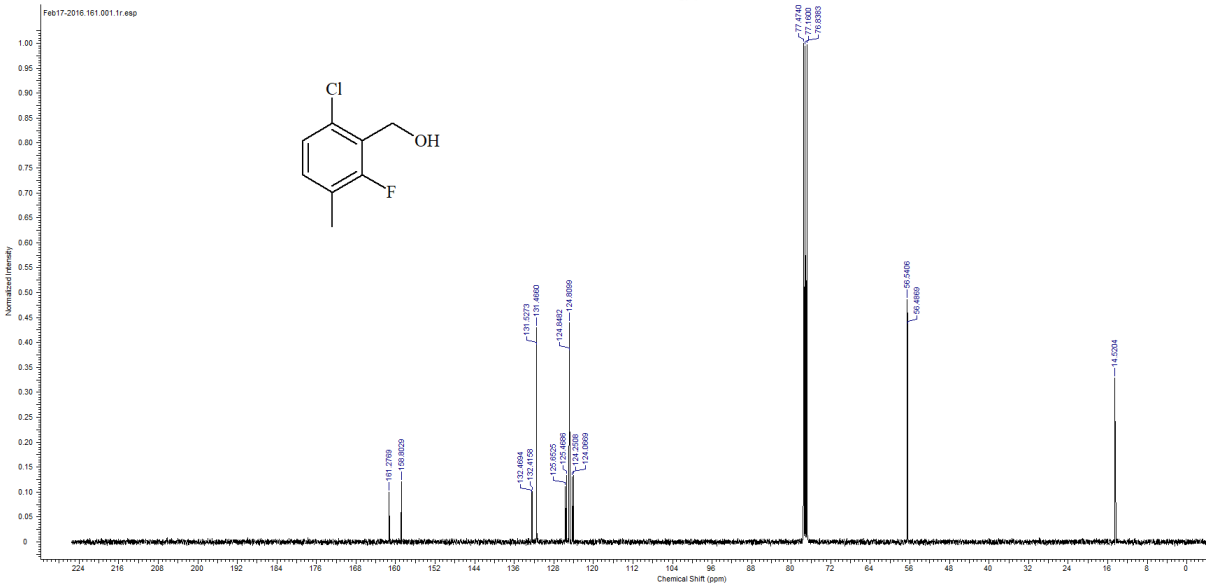

Feb03-2016.150.001.1r.esp
F
OH
Cl
Normalized Intensity
Chemical Shift (ppm)

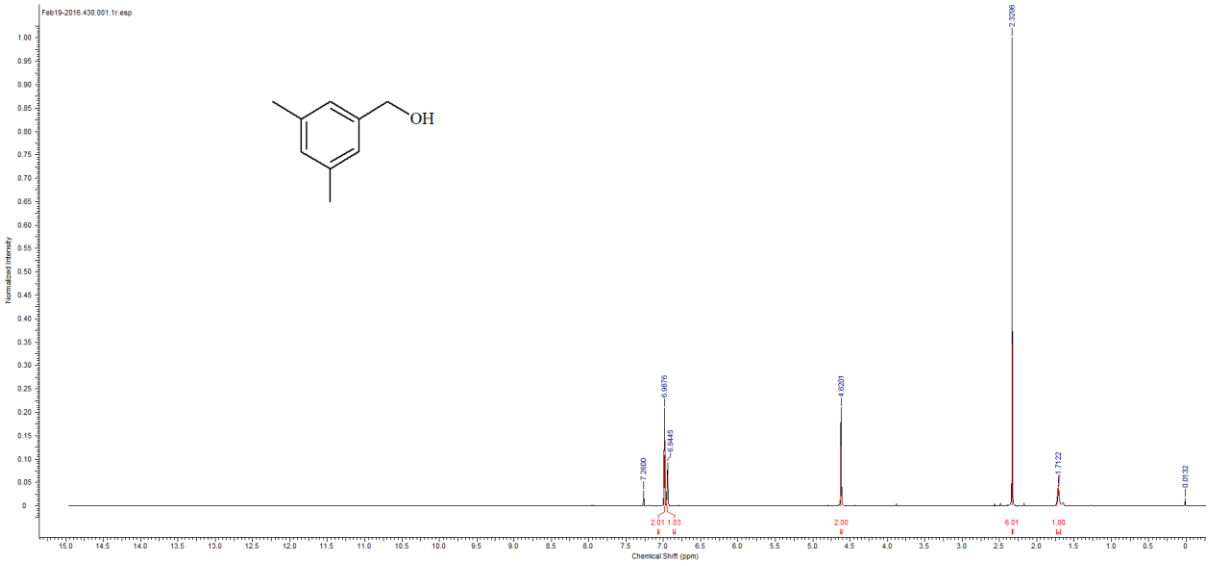

Feb03-2016.151.001.1r.esp
F
OH
Cl
Normalized Intensity
Chemical Shift (ppm)

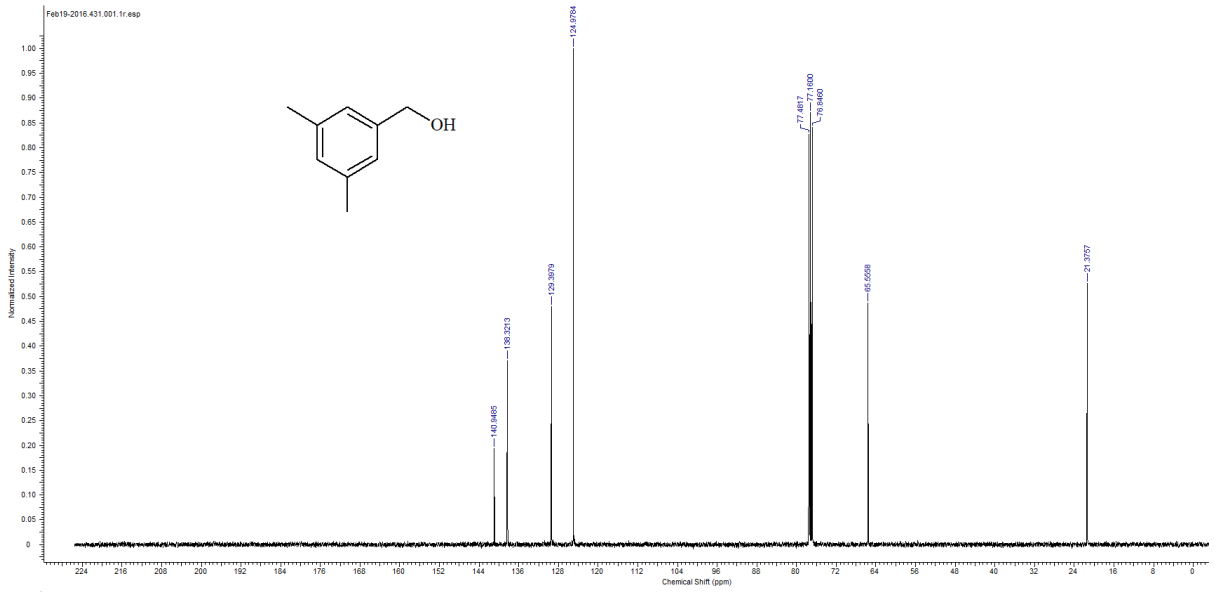

Feb03-2016.130.001.1r.esp
OH
Cl
Cl
Normalized Intensity
Chemical Shift (ppm)

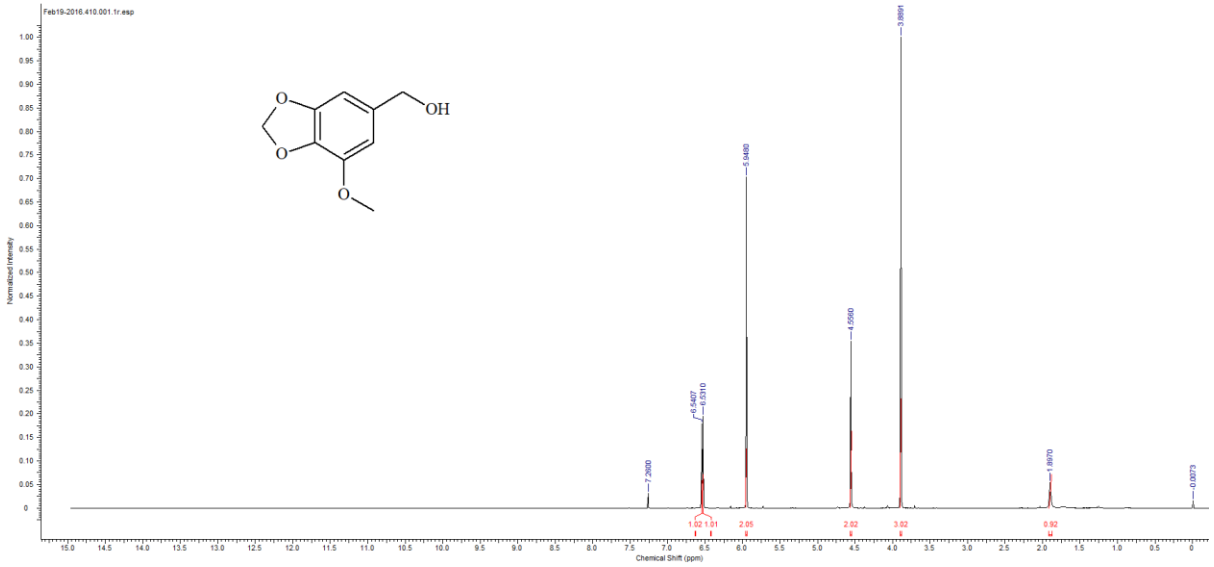

Feb03-2016.131.001.1r.esp
OH
Cl
Cl
Normalized Intensity
Chemical Shift (ppm)

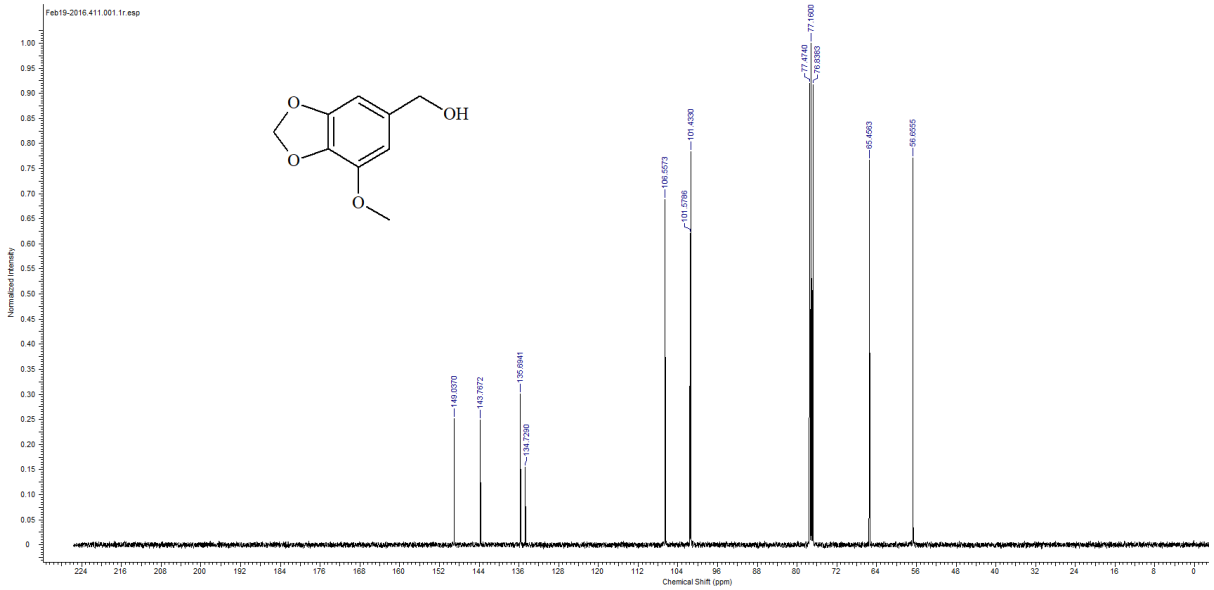

Aug31-2018.040.001.1r.esp
Cl
OH
F
Normalized Intensity
Chemical Shift (ppm)

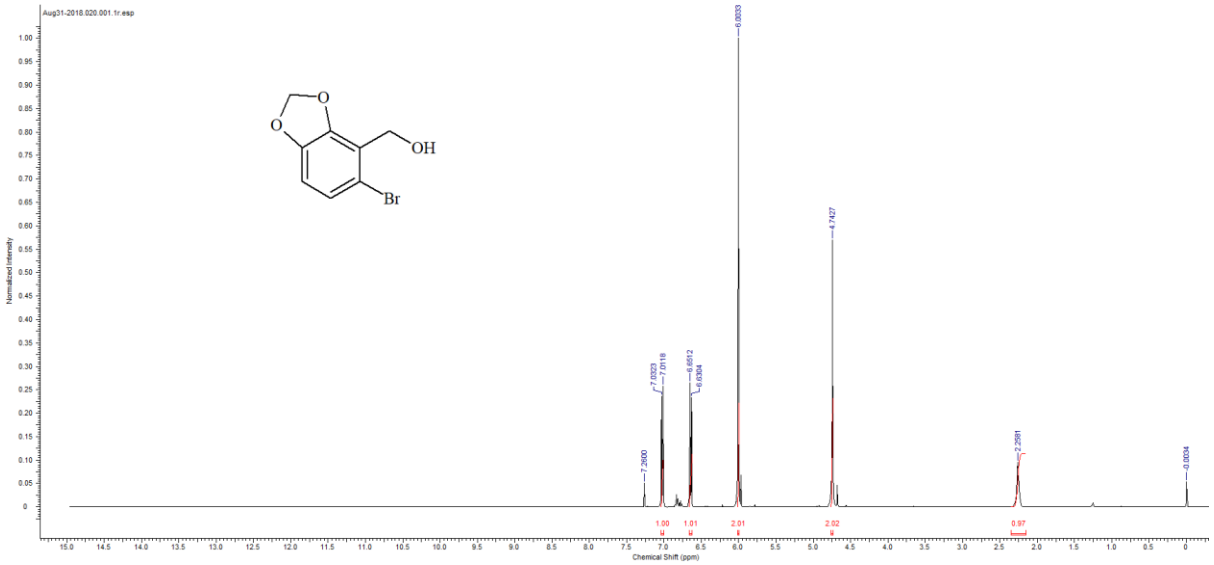

Feb17-2016.161.001.1r.esp
Cl
OH
F
Normalized Intensity
Chemical Shift (ppm)

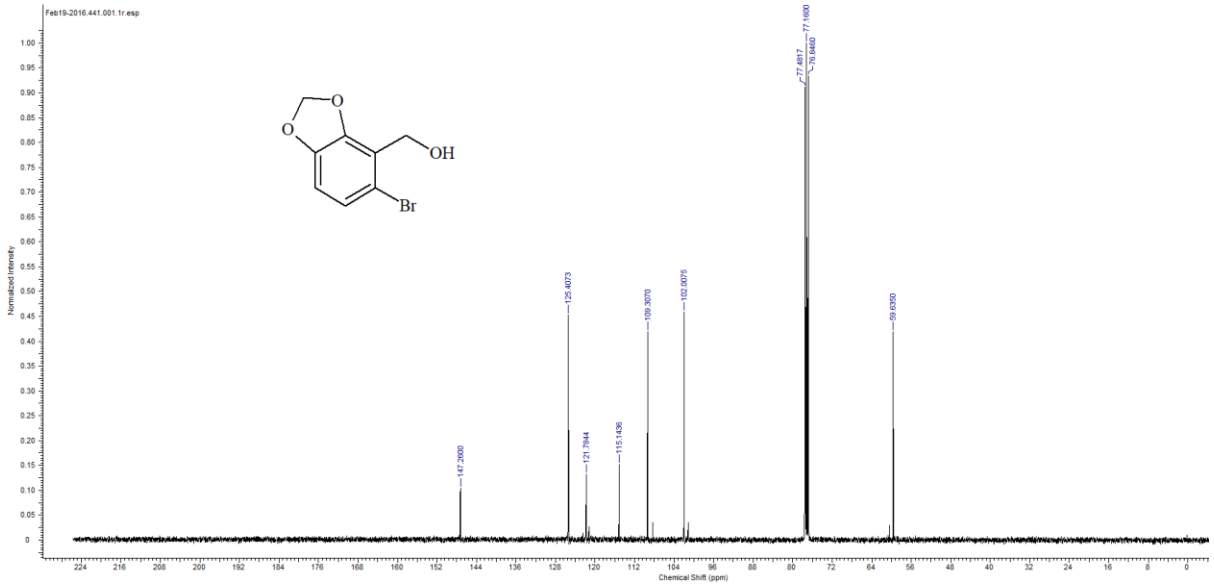

Feb19-2016.430.001.1r.esp
OH
Normalized Intensity
Chemical Shift (ppm)

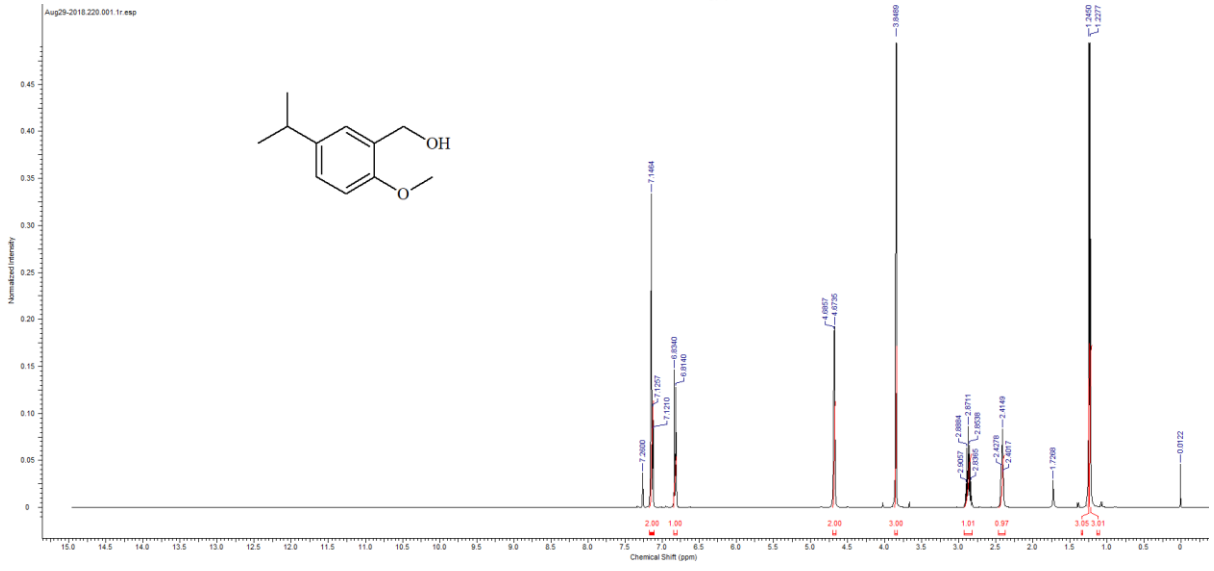

Feb19-2016.431.001.1r.esp
OH
Normalized Intensity
Chemical Shift (ppm)
140.9485
138.3213
129.3679
124.9784
77.4817
77.1600
76.8468
65.5558
21.3757

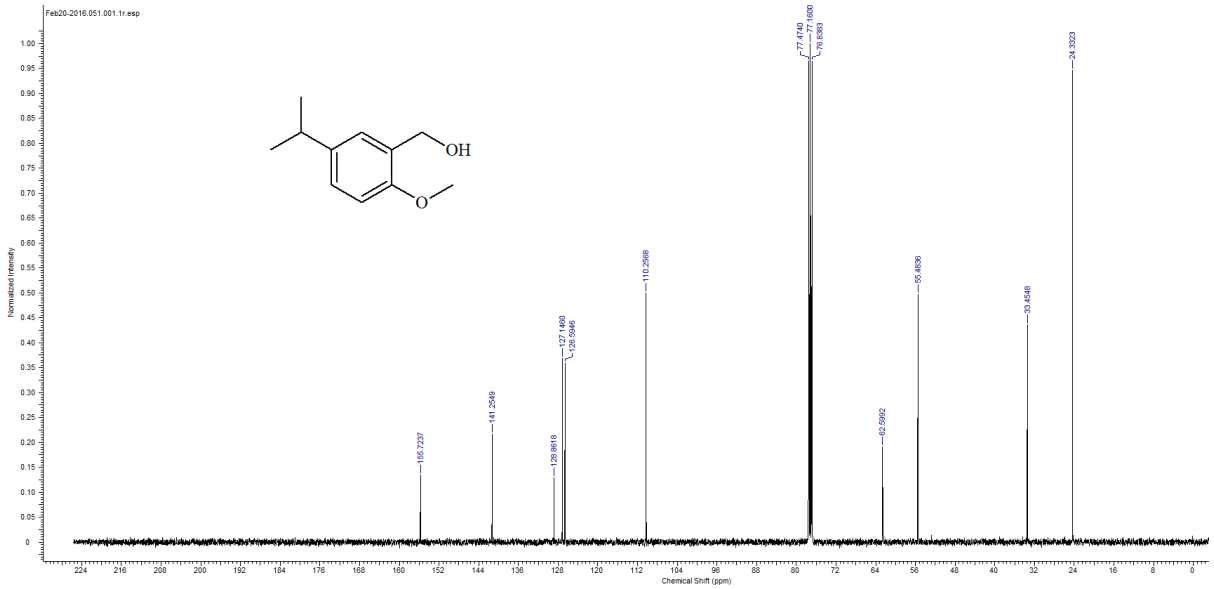

Feb19-2016.410.001.1r.esp
O
O
OH
O
Normalized Intensity
Chemical Shift (ppm)
7.2800
6.5407
6.5310
5.9480
4.2560
3.8891
1.8970
0.0373
1.02
1.01
2.05
2.02
3.02
0.92

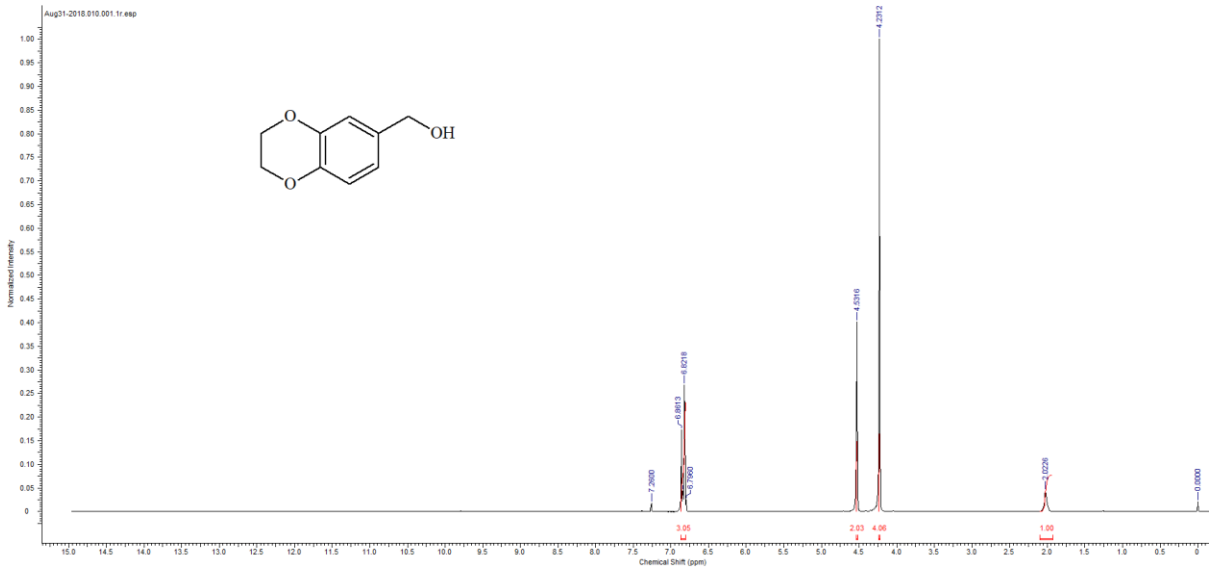

Feb19-2016.411.001.1r.esp
O
O
OH
O
Normalized Intensity
Chemical Shift (ppm)
149.0370
143.7672
135.6941
134.7260
106.5573
101.4330
101.5798
77.4740
77.1600
76.8383
65.4563
56.6555

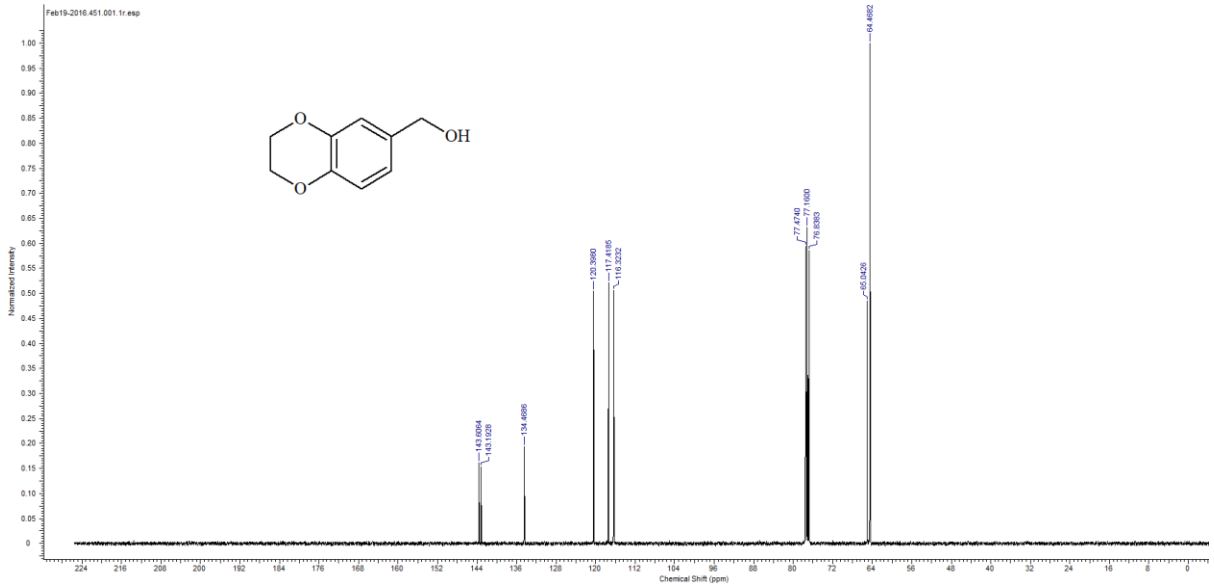

Aug31-2018.020.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
OH
Br
7.2600
7.0023
7.0018
6.8812
6.6304
6.0033
4.7427
2.2991
0.0034
1.00
1.01
2.01
2.02
0.97


Feb19-2016.441.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
OH
Br
147.2000
125.4073
121.7844
115.1436
109.3070
102.0075
77.4817
77.1600
76.8460
59.6350

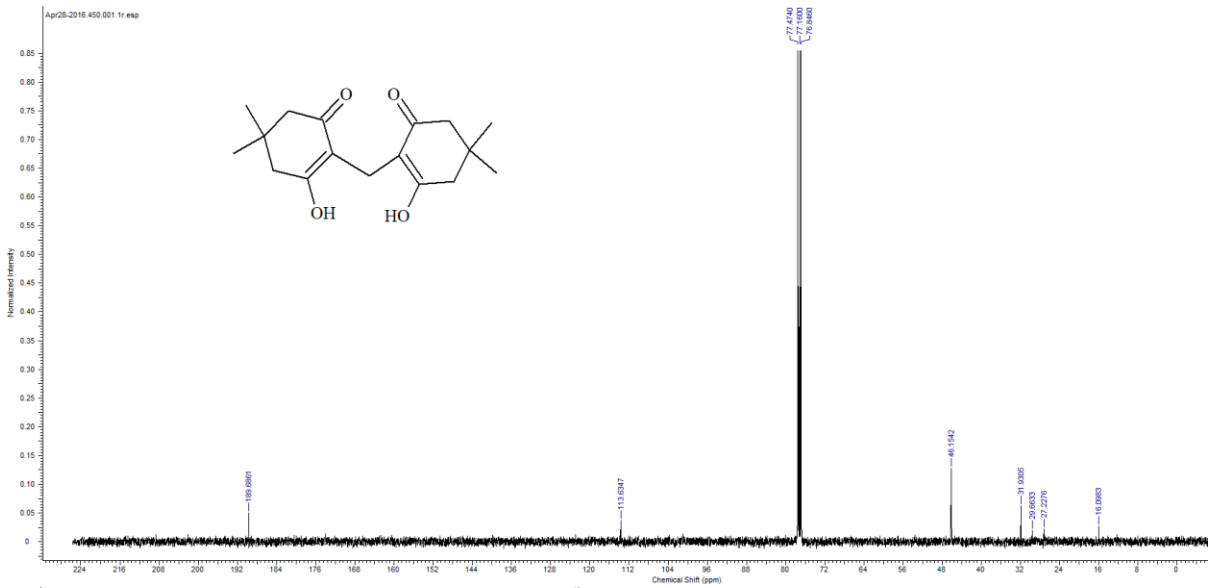

Aug29-2018.220.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
OH
O
7.2600
7.1464
7.1257
7.1210
6.8340
6.8140
4.9957
4.9725
3.8489
2.9057
2.8884
2.8711
2.8386
2.8038
2.4278
2.4149
2.4017
1.7209
1.3459
1.3237
0.0122
2.00
1.00
2.00
3.00
1.01
0.97
3.05
3.01


Feb20-2016.051.001.1r.esp
OH
O
Normalized Intensity
Chemical Shift (ppm)
155.7237
141.2549
139.8818
127.1460
126.5946
110.2566
77.4740
77.1600
76.8393
82.5992
55.4636
33.4548
24.3323


Aug31-2018.010.001.1r.esp
O
O
OH
Normalized Intensity
Chemical Shift (ppm)
7.2800
6.8613
6.8218
6.7960
4.5316
4.2312
3.8226
0.0000
3.05
2.03
4.06
1.00

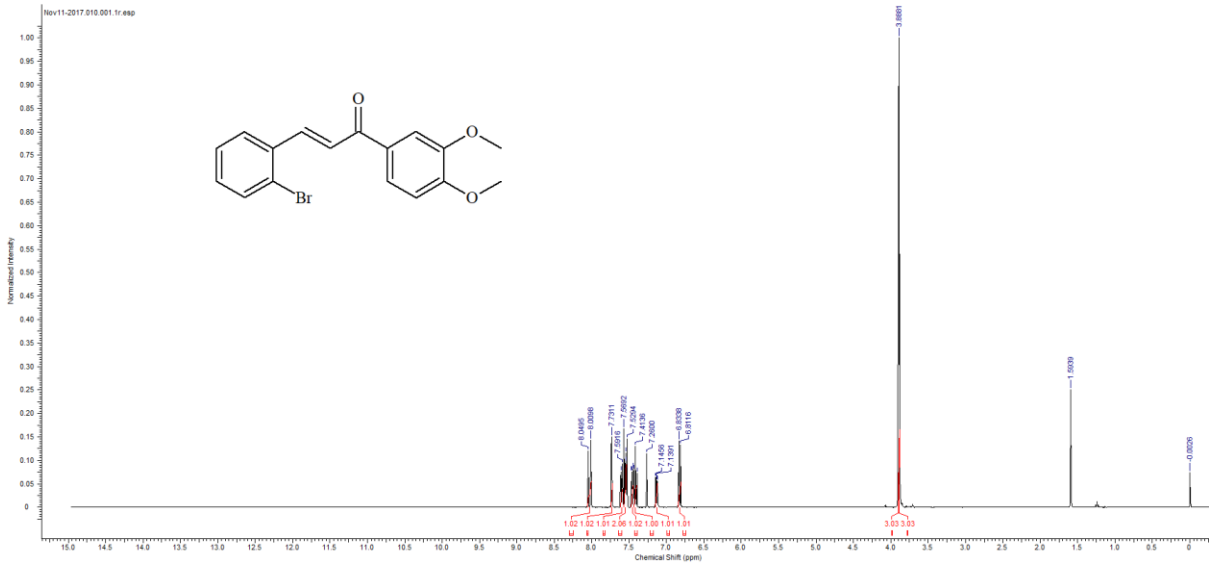

Feb19-2016.451.001.1r.esp
O
O
OH
Normalized Intensity
Chemical Shift (ppm)
143.6064
143.1928
134.4686
120.3980
117.4186
116.3232
77.4740
77.1600
76.8393
65.0426
64.4682

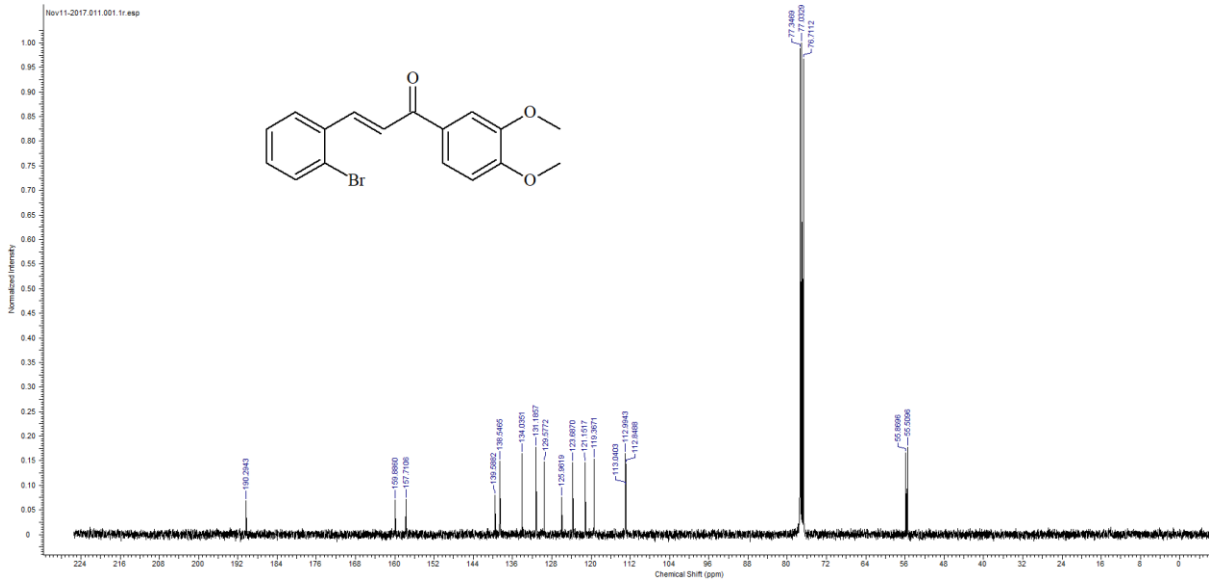

Apr27-2016.300.001.1r.esp
O
O
OH
HO
Normalized Intensity
Chemical Shift (ppm)
11.5999
7.2600
3.1598
2.2932
2.2813
1.5881
1.0590
0.0012
2.00
2.03
8.02
12.04

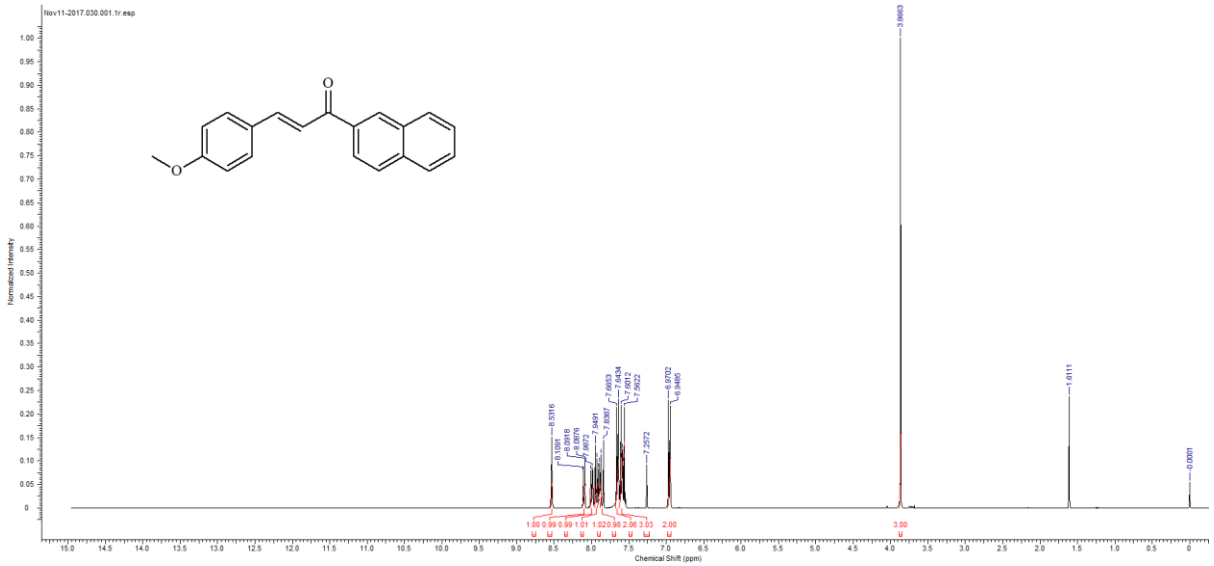

Apr28-2016.450.001.1r.esp
O
O
OH
HO
Normalized Intensity
Chemical Shift (ppm)
77.4740
77.1600
76.8460
189.6861
113.6347
46.1542
31.9065
29.9633
27.2276
16.0863

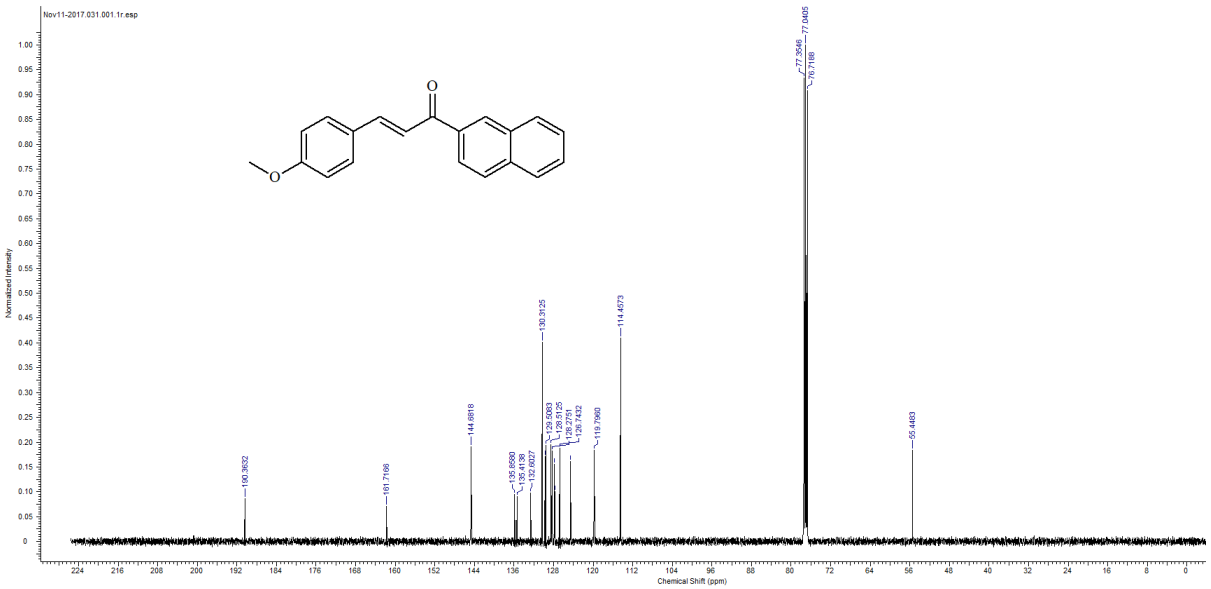

Apr28-2016.520.001.1r.esp
H
D
OD
NO2
Normalized Intensity
Chemical Shift (ppm)
8.2209
8.1995
7.5411
7.5199
7.2600
4.8339
2.0355
1.2499
0.0009
2.07
2.01
1.10

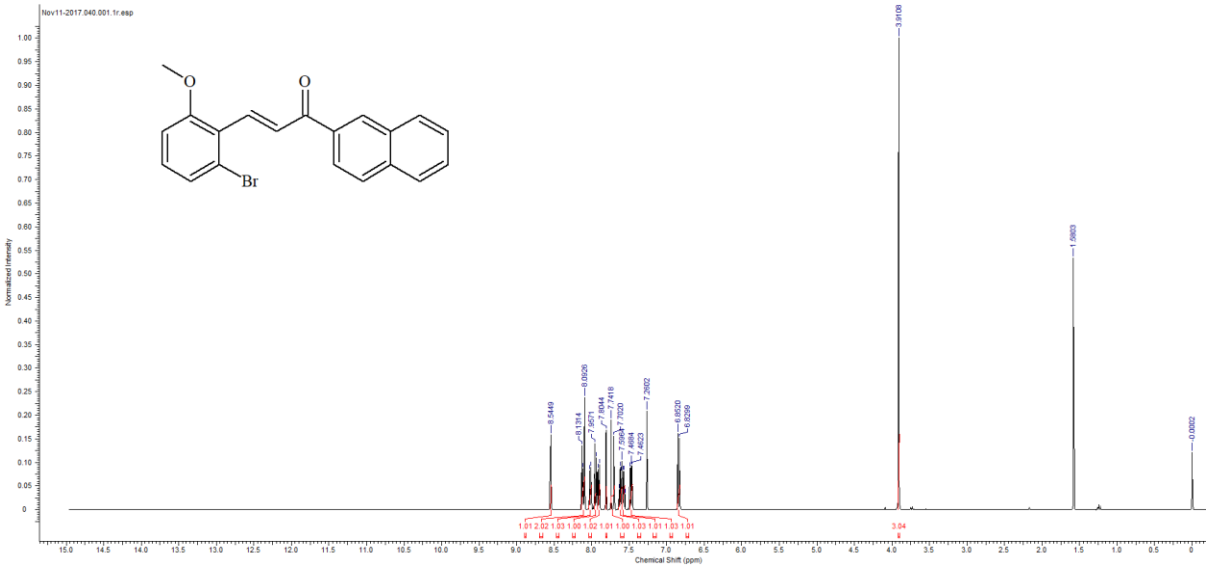
Copies of NMR spectra for the synthesis of unsaturated ketones

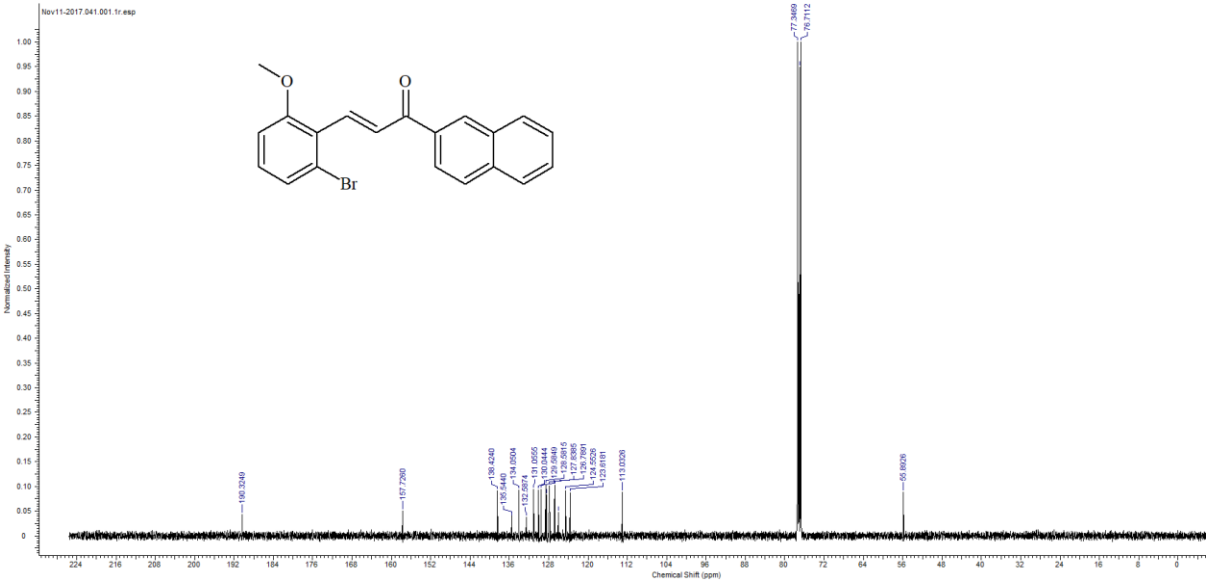


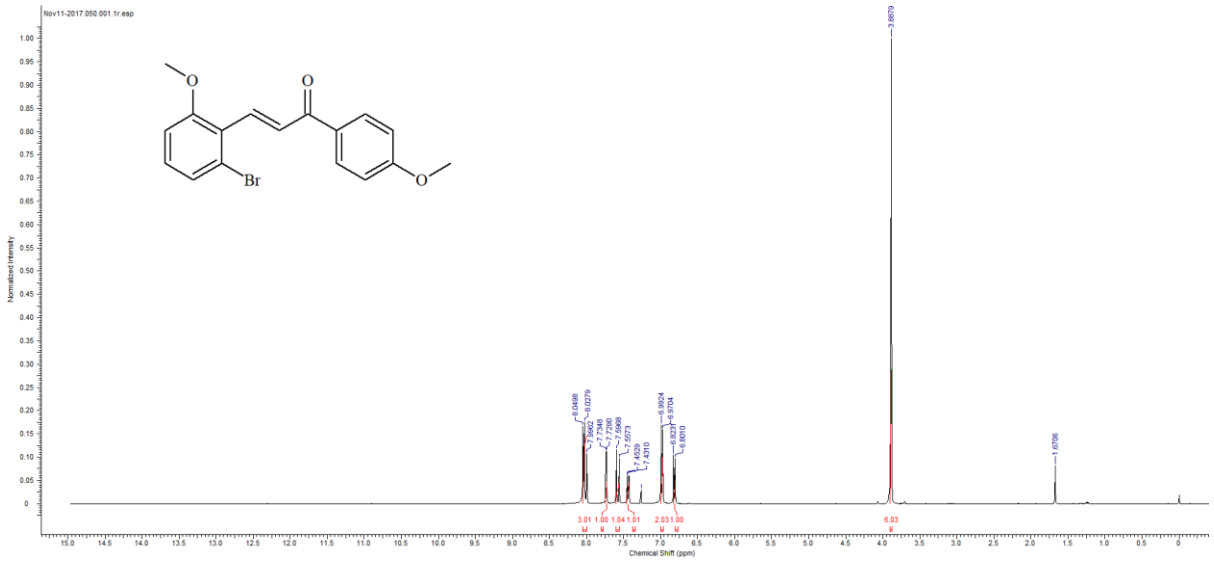


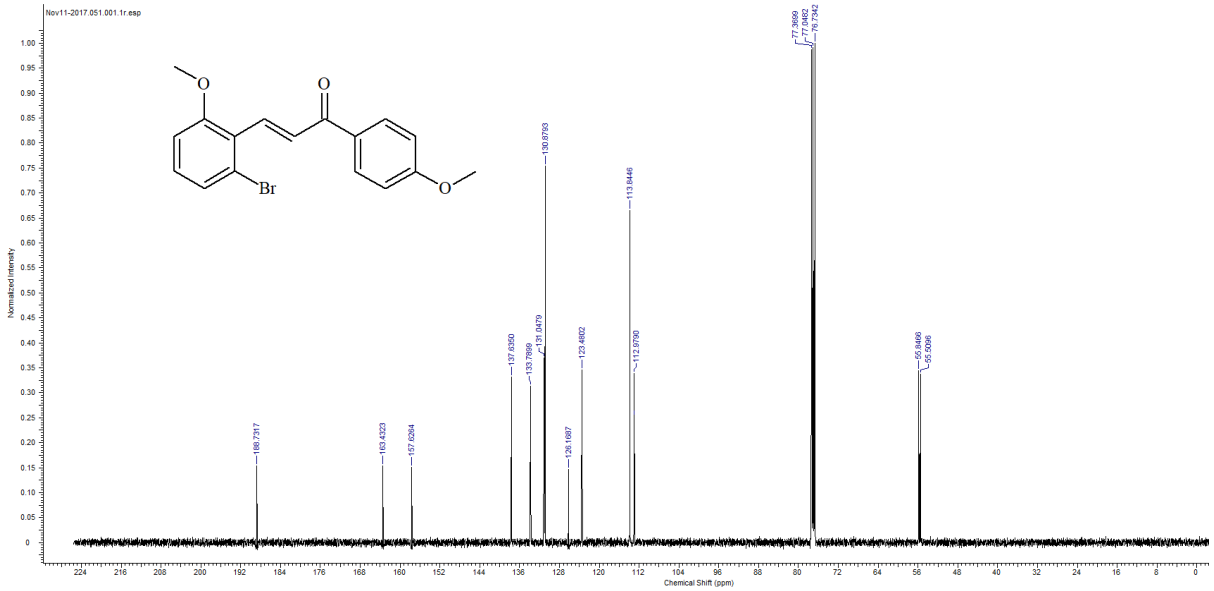


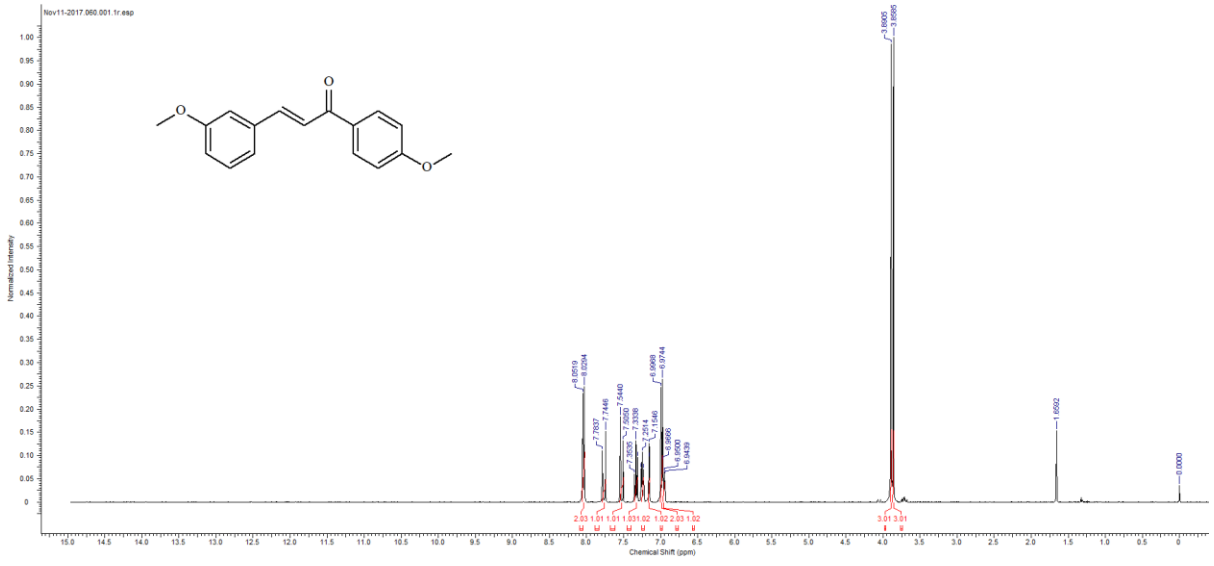

Nov11-2017.031.001.1r.esp
O
O
77.3546
77.0405
76.7168
130.3125
114.4573
144.6818
129.0303
128.9125
128.2731
128.0742
119.7960
55.4483
190.3632
181.7166
135.8590
135.1438
132.0027
Normalized Intensity
Chemical Shift (ppm)

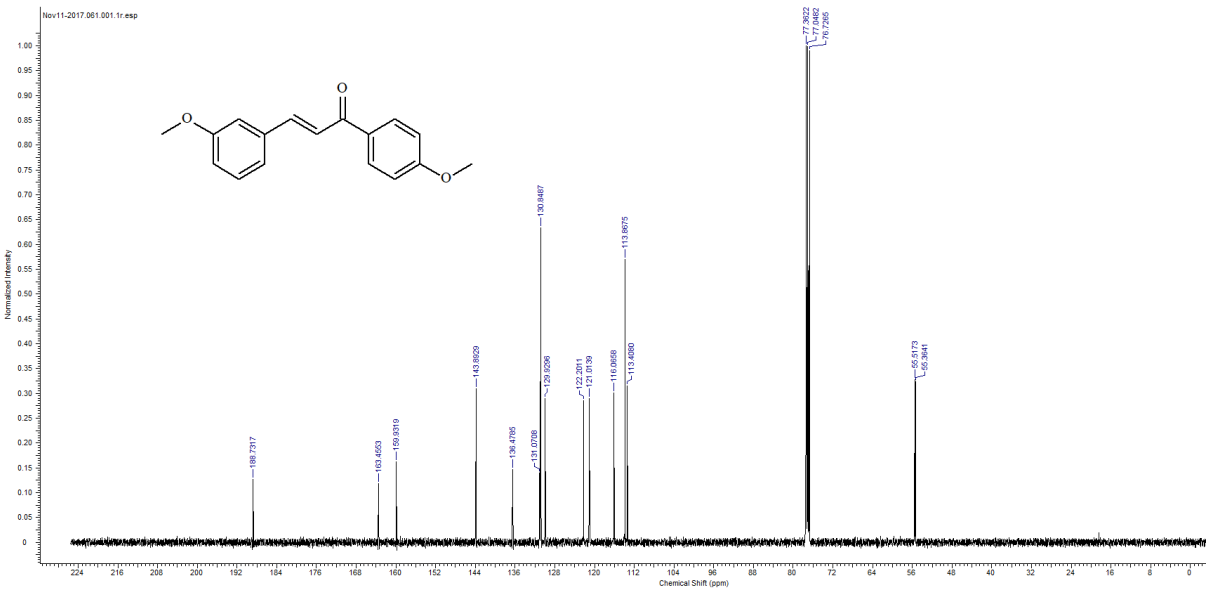

Nov11-2017.040.001.1r.esp
O
O
Br
3.9108
1.9803
8.0926
8.5449
8.1394
7.8671
7.8044
7.7418
7.7003
7.5993
7.4894
7.4623
7.2902
6.8820
6.8259
0.0002
1.01 2.02 1.03 1.00 1.02 1.01 1.00 1.03 1.01 1.03 1.01
3.04
Normalized Intensity
Chemical Shift (ppm)

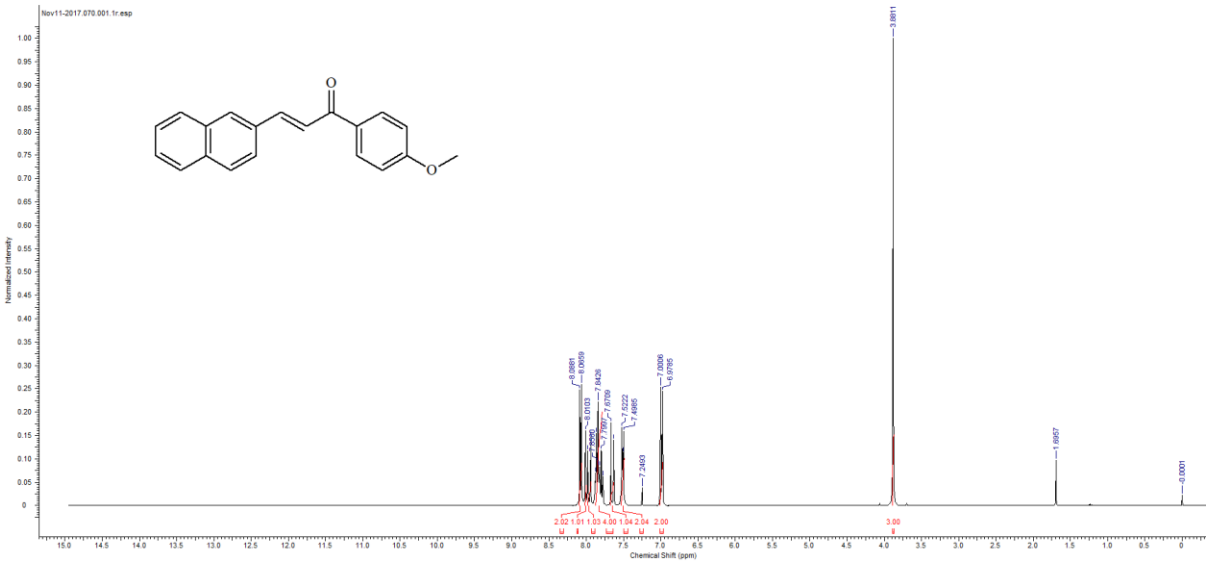

Nov11-2017.041.001.1r.esp
O
O
Br
77.3469
76.7112
138.4240
135.5440
134.0504
131.0955
130.0444
129.8981
128.8845
127.8385
126.7891
126.4578
123.6818
113.0326
55.8926
190.3249
157.7260
Normalized Intensity
Chemical Shift (ppm)

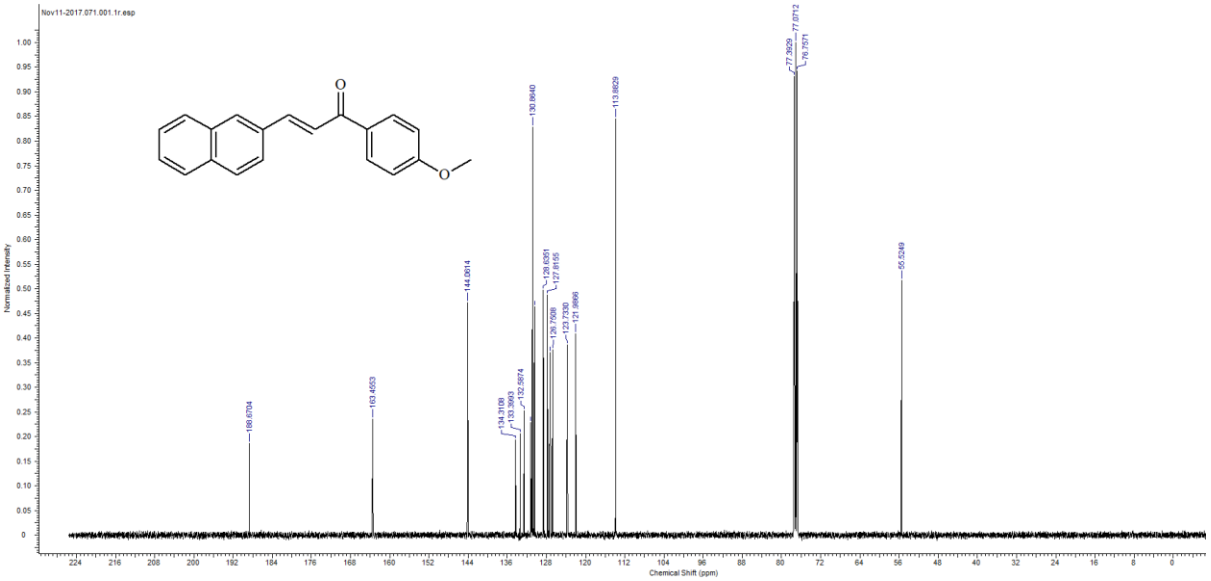

Nov11-2017.050.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
O
Br
O
8.0498
8.0279
7.9662
7.7748
7.7568
7.5968
7.5573
7.4529
7.4310
6.9924
6.9704
6.8237
6.8010
3.8879
1.6708
3.01 1.00 1.04 1.01 2.03 1.00
6.03

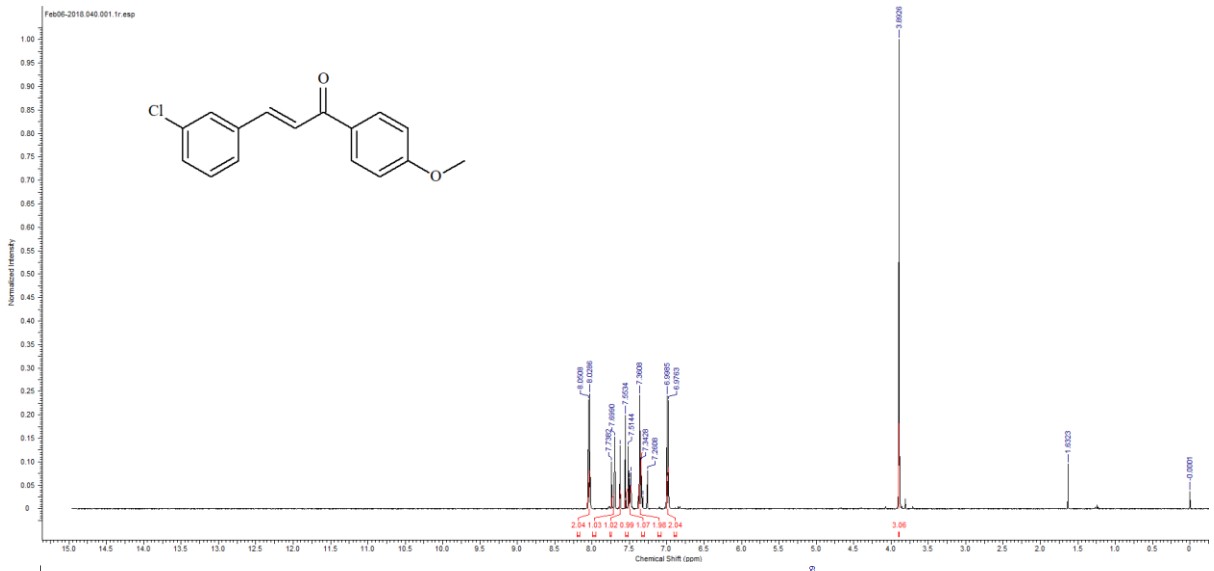

Nov11-2017.051.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
O
Br
O
77.3699
77.0482
76.7342
130.8793
113.8446
137.6350
133.7959
131.0479
123.4802
112.6790
126.1687
189.7317
163.4323
157.6284
55.8466
55.5098

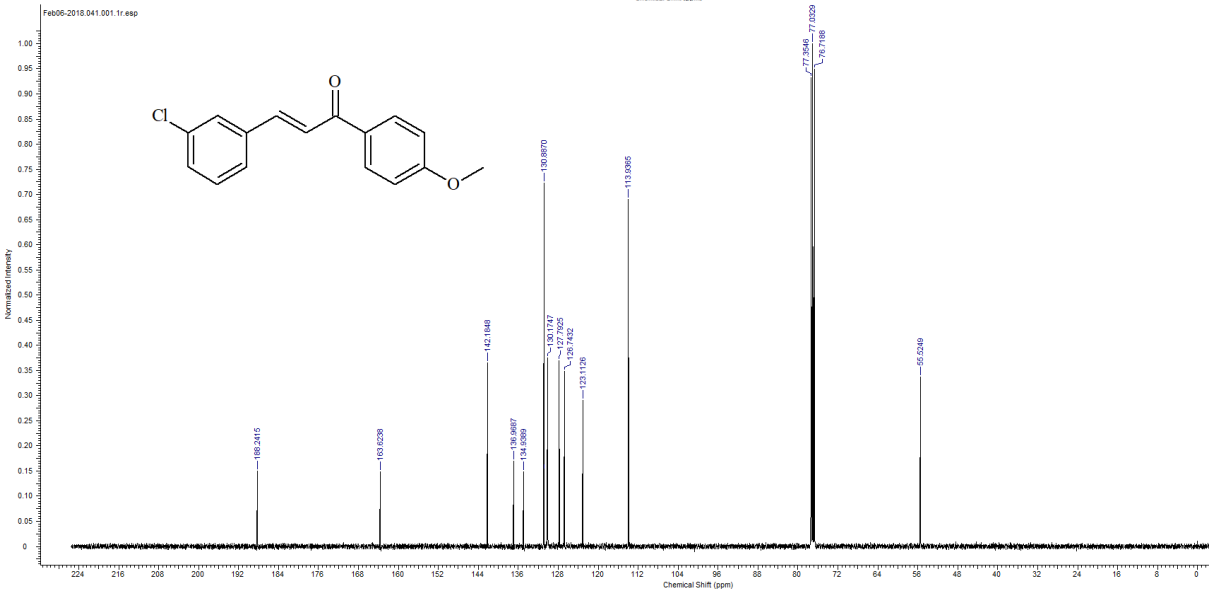

Nov11-2017.060.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
O
O
8.0519
8.0294
7.7957
7.7446
7.5440
7.3936
7.3535
7.2514
7.1546
6.9666
6.9503
6.9439
8.0069
8.0744
3.8905
3.8585
1.6592
8.0000
2.03 1.01 1.01 1.03 1.02 1.02 2.03 1.02
3.01 3.01

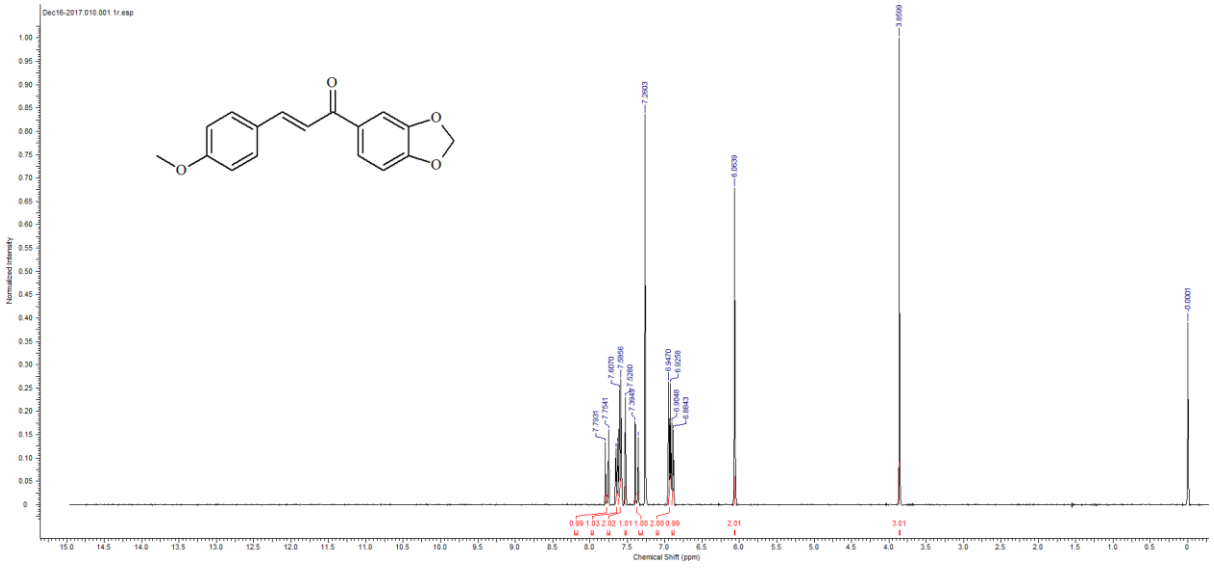

Nov11-2017.061.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
188.7317
163.4553
159.9319
143.8029
136.4795
131.0708
130.9467
129.8296
122.2011
121.0139
116.0658
113.8675
113.4080
77.3922
77.0802
76.7265
55.5173
55.3641

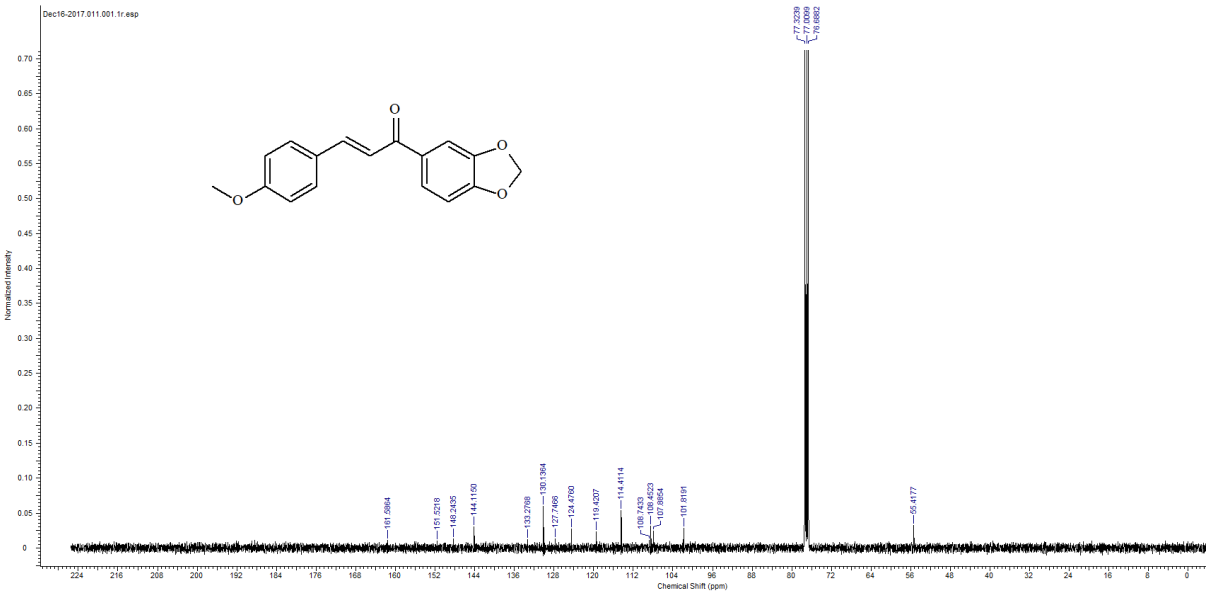

Nov11-2017.070.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
8.0861
8.0659
8.0103
7.9426
7.9109
7.8997
7.8789
7.6222
7.6065
7.2493
7.0006
6.9785
3.8911
1.9957
0.0001
2.02 1.01 1.03 4.00 1.04 2.04 2.00
3.00

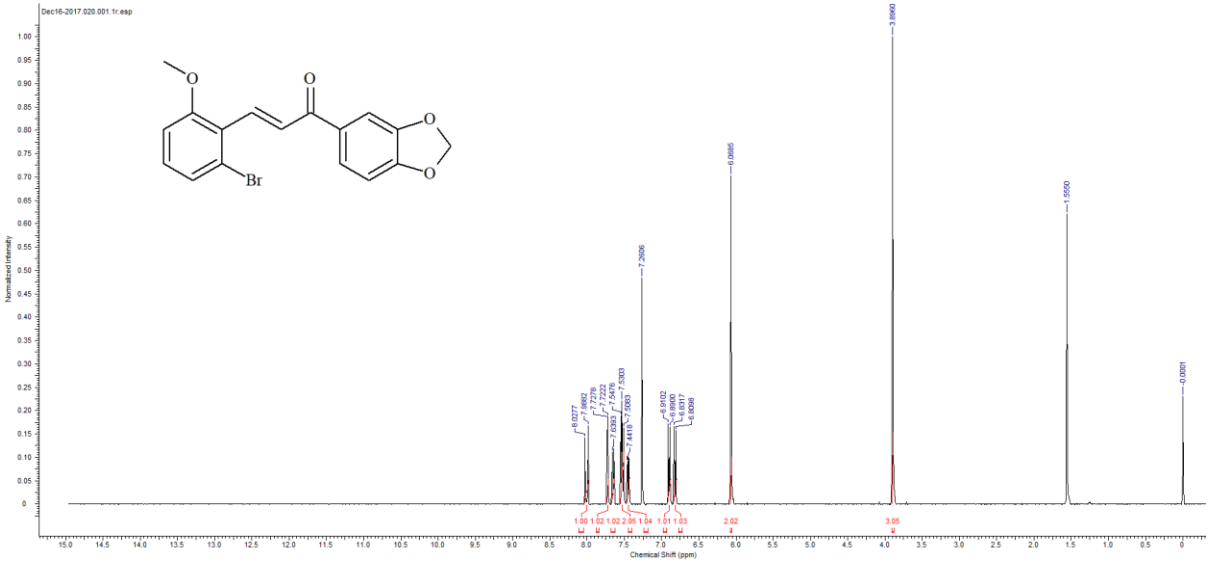

Nov11-2017.071.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
188.6704
163.4553
144.0814
134.3199
133.3963
132.9874
130.8640
129.8351
127.8165
126.7508
123.7099
121.9999
113.8629
77.3929
77.0712
76.7571
55.5249

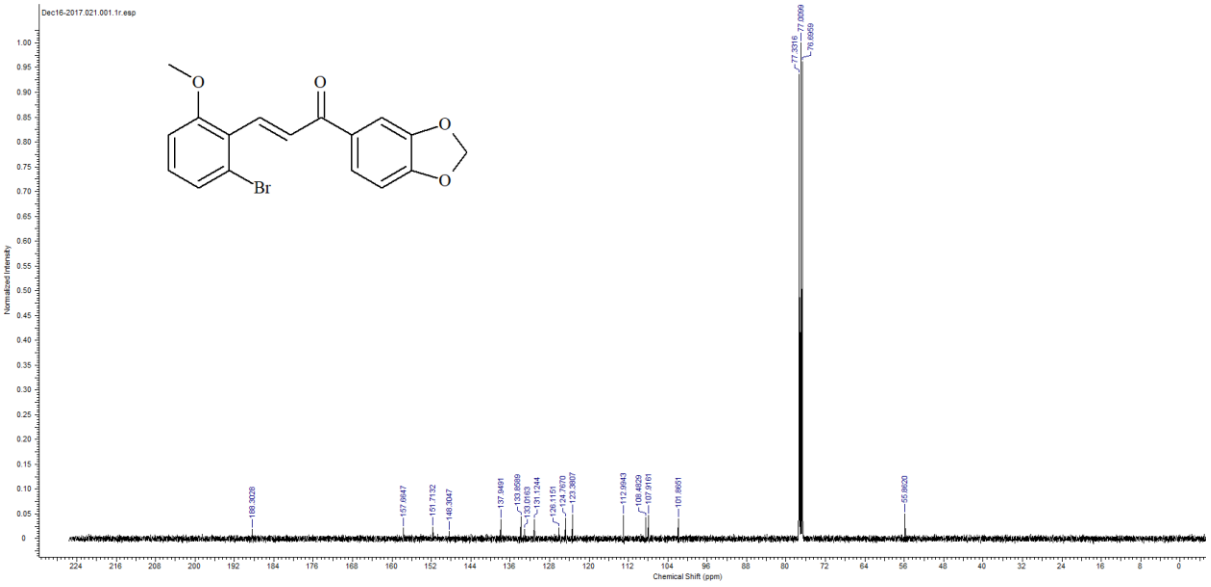

Feb06-2018.040.001.1r.esp
Cl
O
O
Normalized Intensity
Chemical Shift (ppm)

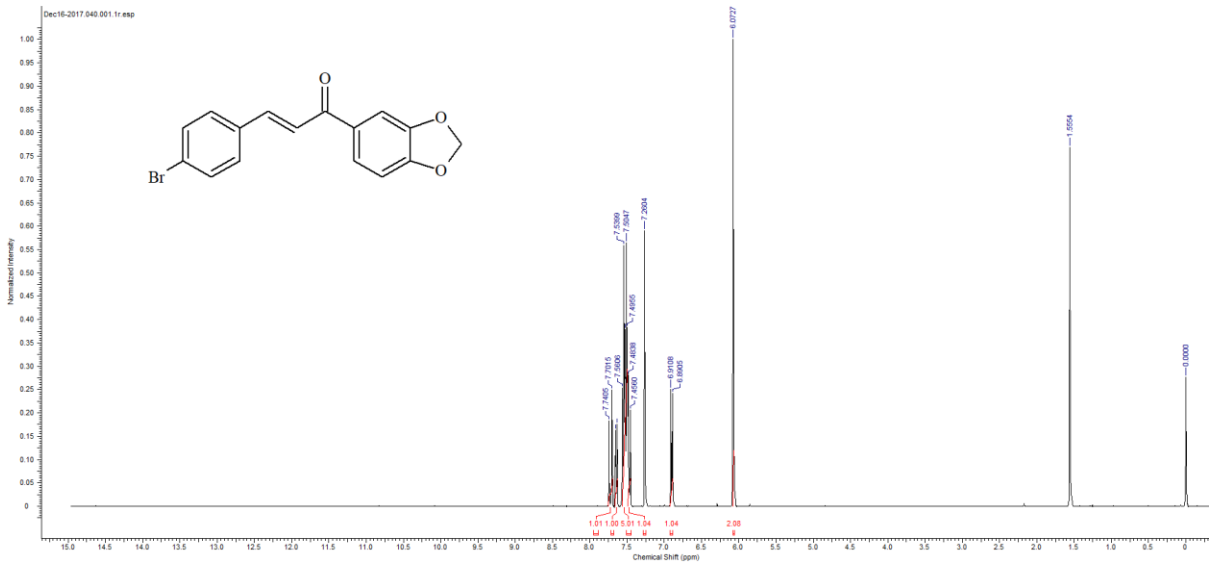

Feb06-2018.041.001.1r.esp
Cl
O
O
Normalized Intensity
Chemical Shift (ppm)

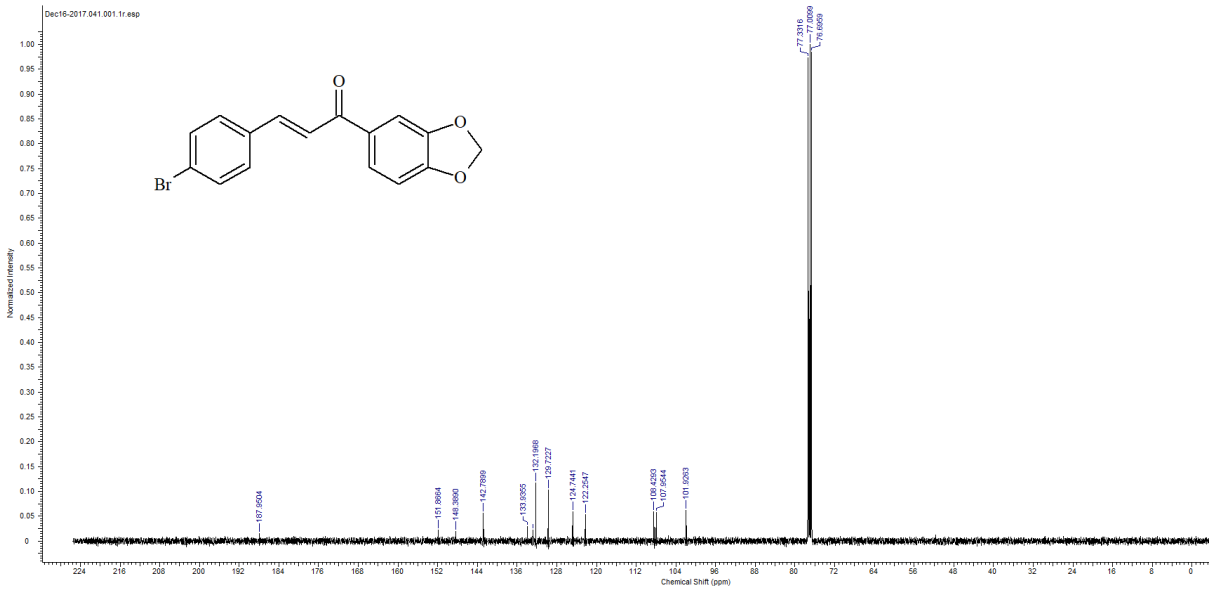

Dec16-2017.010.001.1r.esp
O
O
O
Normalized Intensity
Chemical Shift (ppm)

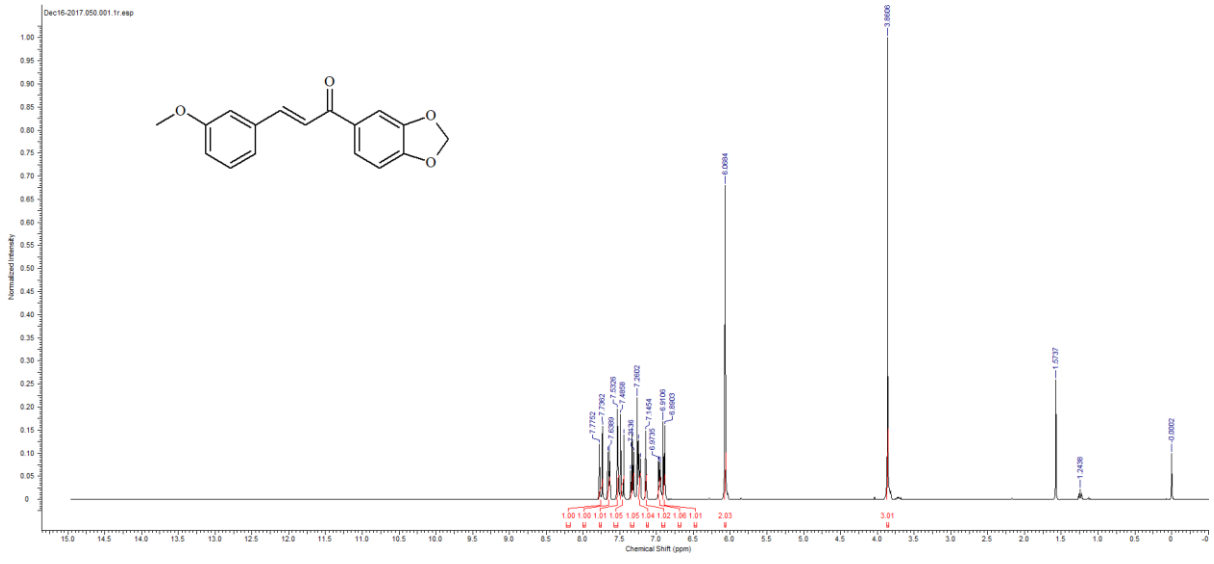

Dec16-2017.011.001.1r.esp
O
O
O
O
Normalized Intensity
Chemical Shift (ppm)

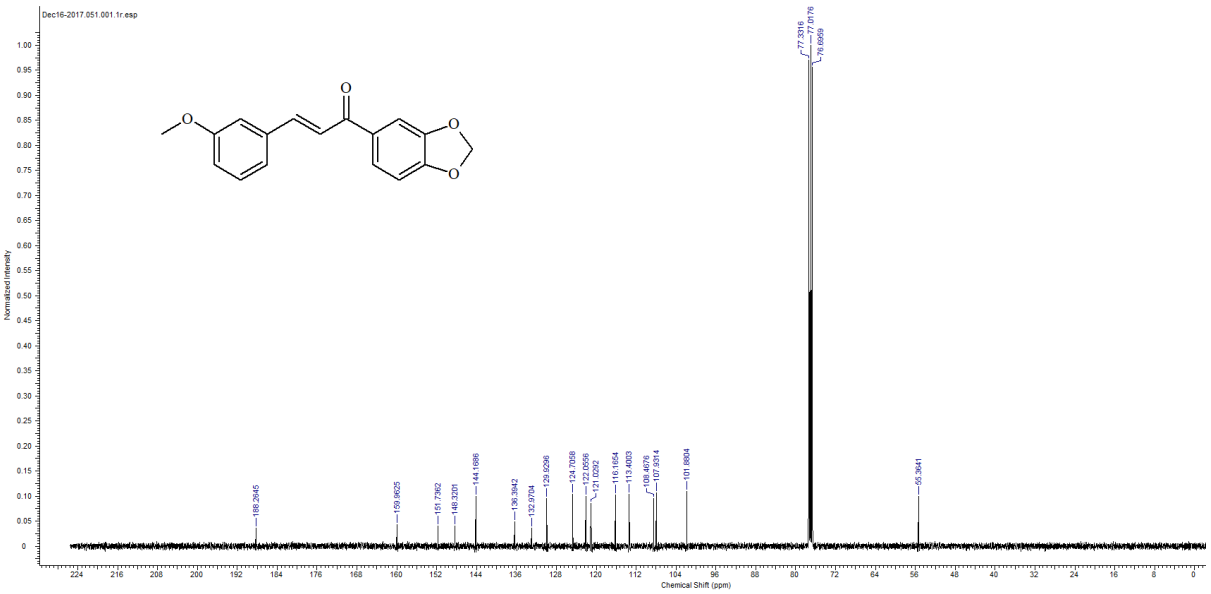

Dec16-2017.020.001.1r.esp
O
O
O
O
Br
Normalized Intensity
Chemical Shift (ppm)

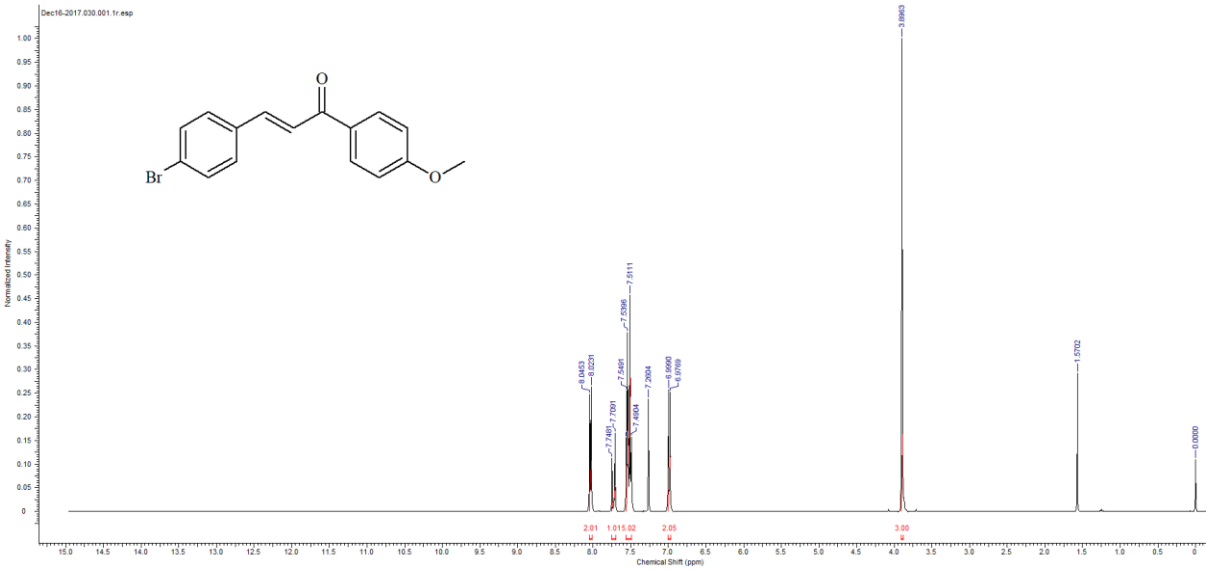

Dec16-2017.021.001.1r.esp
O
O
O
O
Br
Normalized Intensity
Chemical Shift (ppm)

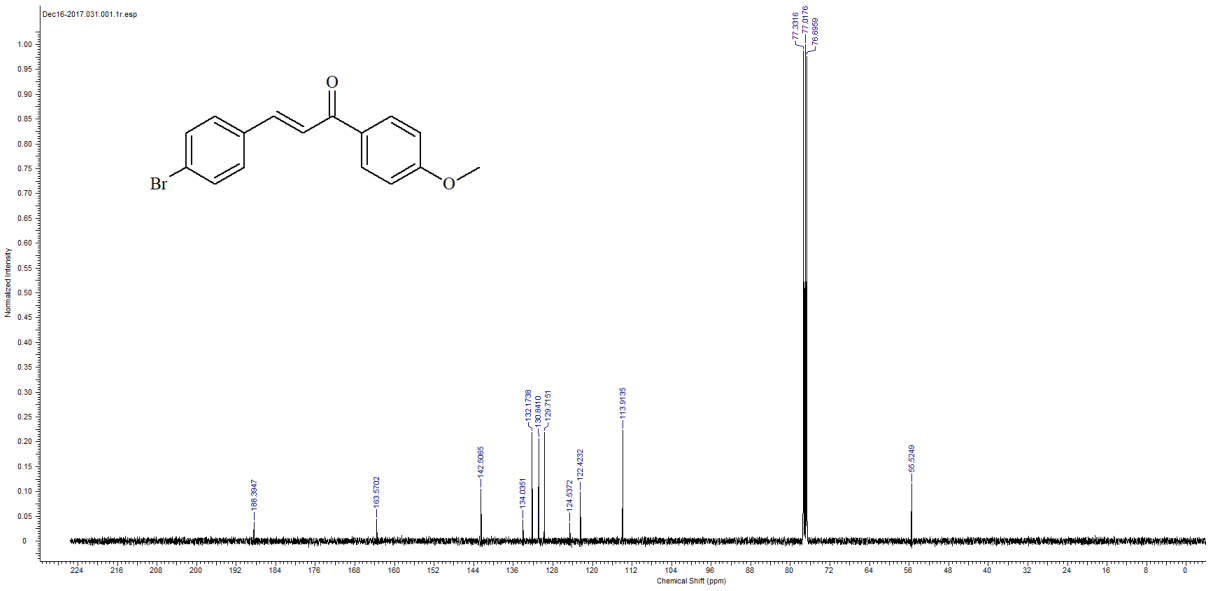

Dec16-2017.040.001.1r.esp
Br
O
O
O
Normalized Intensity
Chemical Shift (ppm)

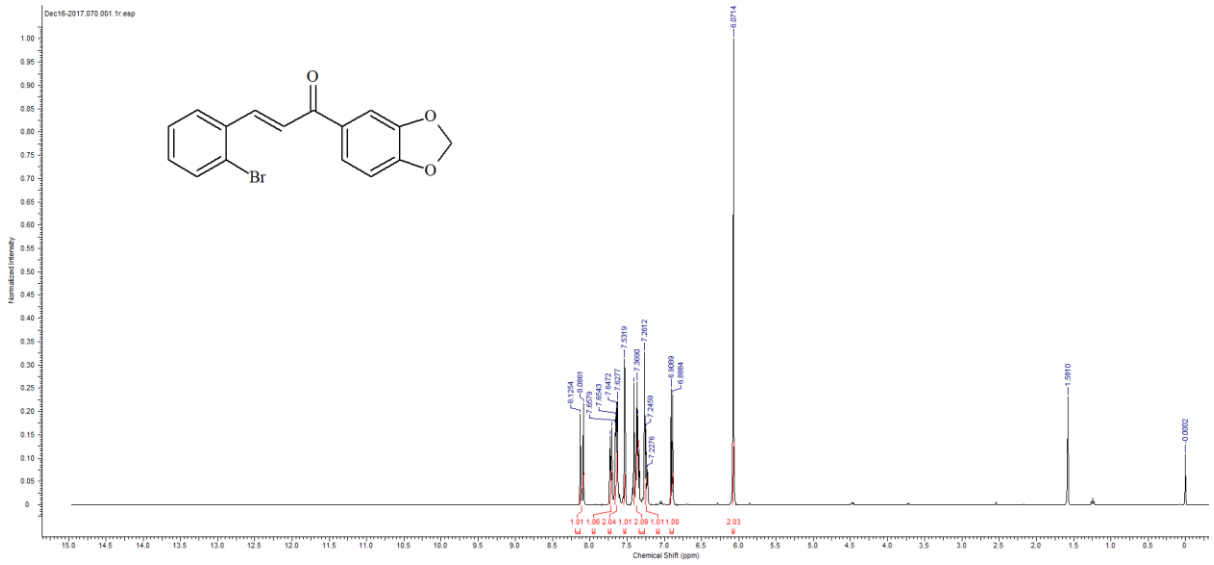

Dec16-2017.041.001.1r.esp
Br
O
O
O
Normalized Intensity
Chemical Shift (ppm)

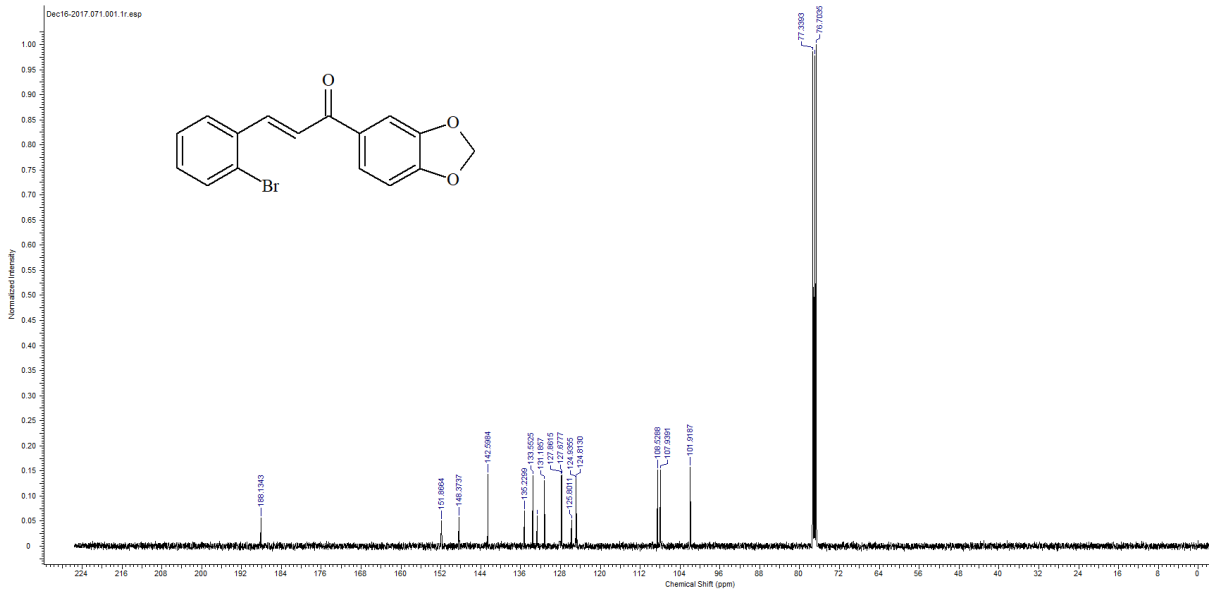

Dec16-2017.050.001.1r.esp
O
O
O
O
Normalized Intensity
Chemical Shift (ppm)

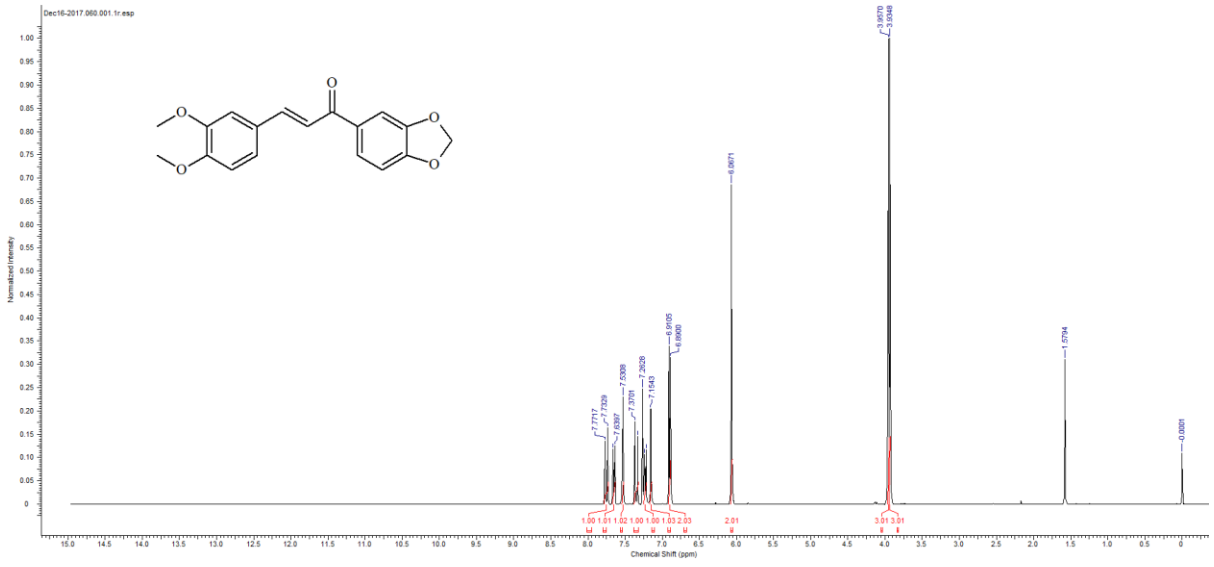

Dec16-2017.051.001.1r.esp
O
O
O
O
Normalized Intensity
Chemical Shift (ppm)
77.3316
77.0176
76.6959
188.2845
159.9625
151.7362
148.3201
144.1686
136.3942
132.9704
129.9296
124.7058
122.0556
121.0292
116.1654
113.4003
108.4676
107.9314
101.8804
55.3641

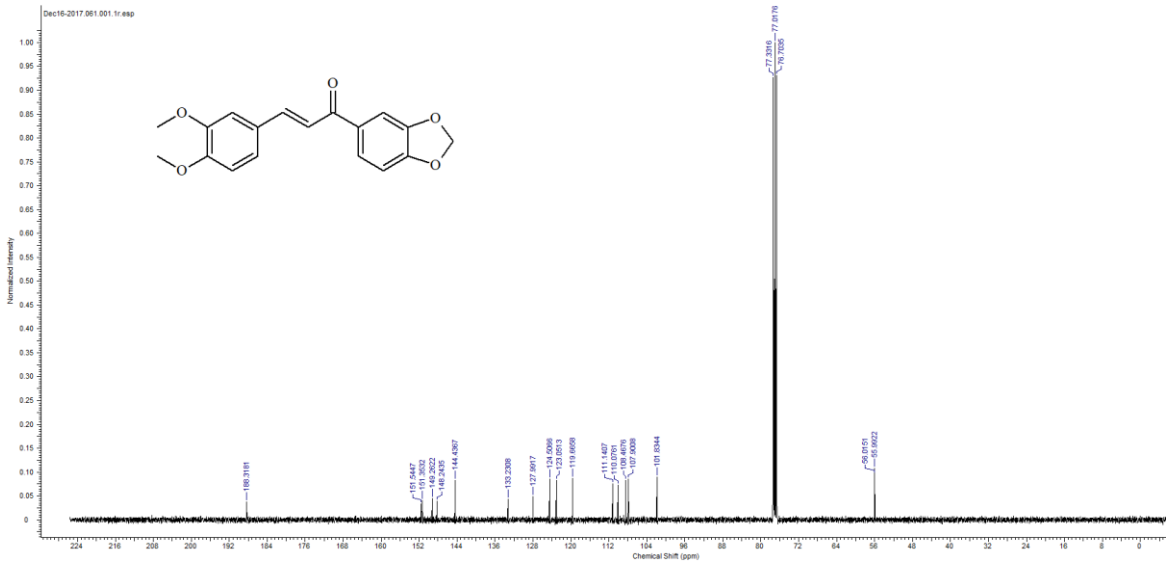

Dec16-2017.030.001.1r.esp
Br
O
O
Normalized Intensity
Chemical Shift (ppm)
3.8863
7.5511
7.5396
8.0455
8.0231
7.5491
7.7091
7.7481
7.5404
7.2604
6.9990
6.9769
1.5702
0.0000
2.01
1.01
5.02
2.05
3.00


Dec16-2017.031.001.1r.esp
Br
O
O
Normalized Intensity
Chemical Shift (ppm)
77.3316
77.0176
76.6959
188.3947
163.6702
142.6065
134.0351
132.1798
130.9510
129.7151
124.5372
122.4232
113.9135
55.5249

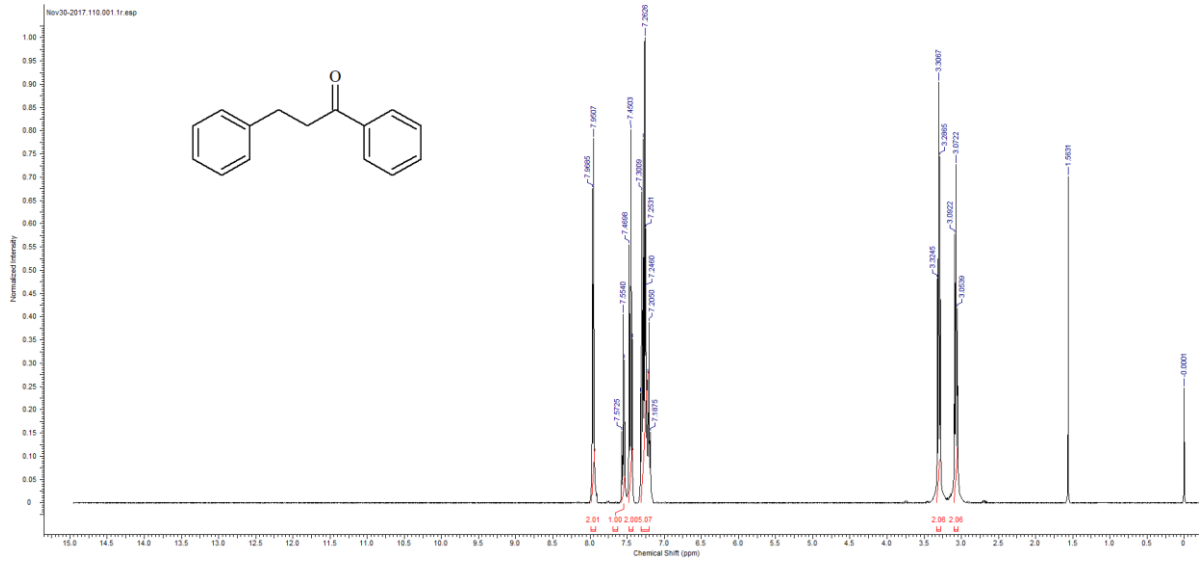

Dec16-2017.070.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
Br
O
O
O
6.0714
1.9810
0.0802

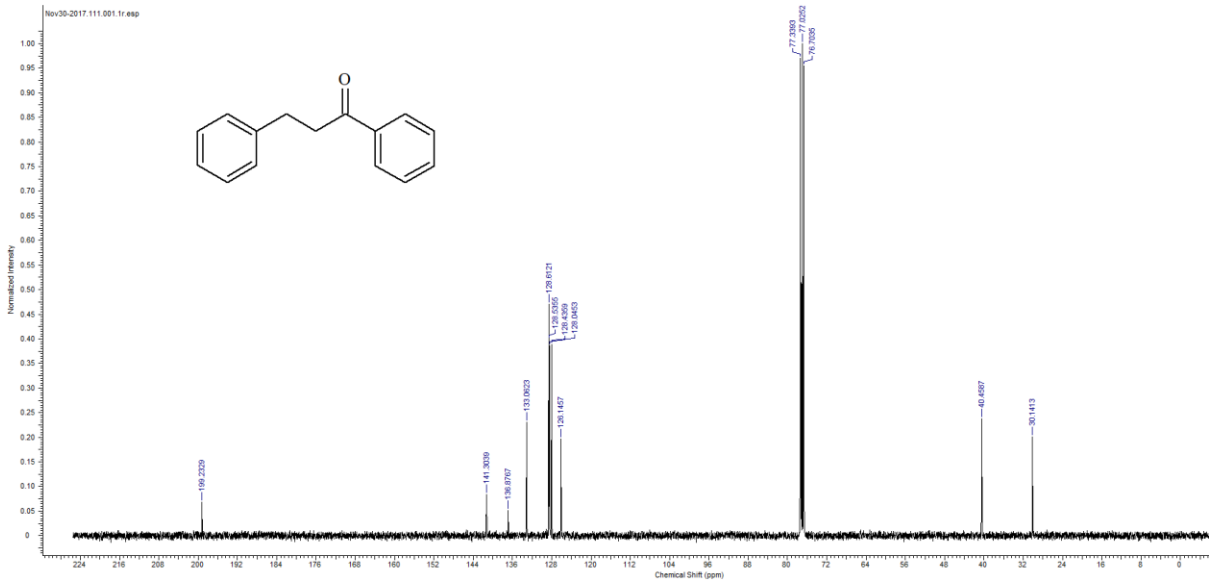

Dec16-2017.071.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
Br
O
O
O
77.3393
76.7035
186.1343
151.8664
148.3737
142.5984
135.2299
133.5525
131.9857
127.8915
127.8777
124.9956
124.8730
125.5811
106.9388
106.9394
101.9187

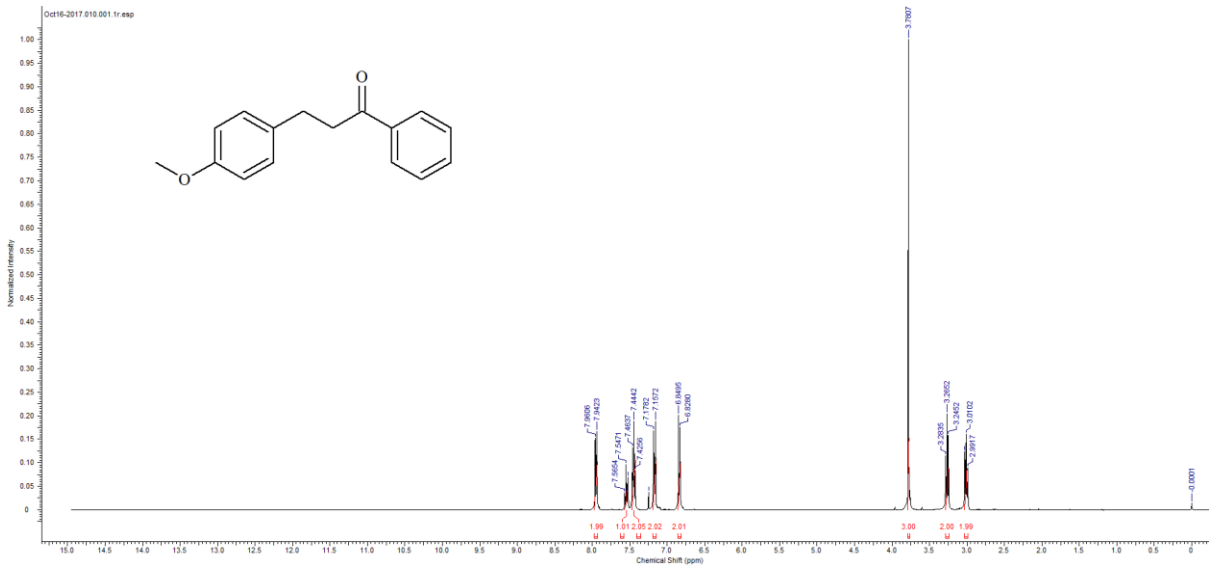

Dec16-2017.060.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
O
O
O
3.9570
3.9568
6.9671
1.5794
0.0001

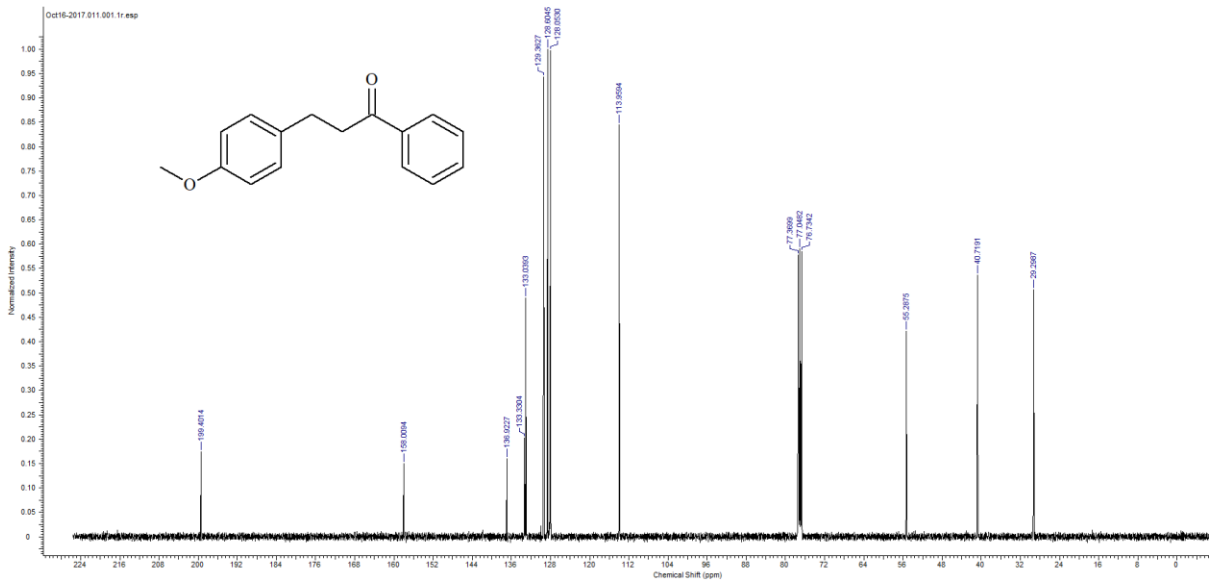


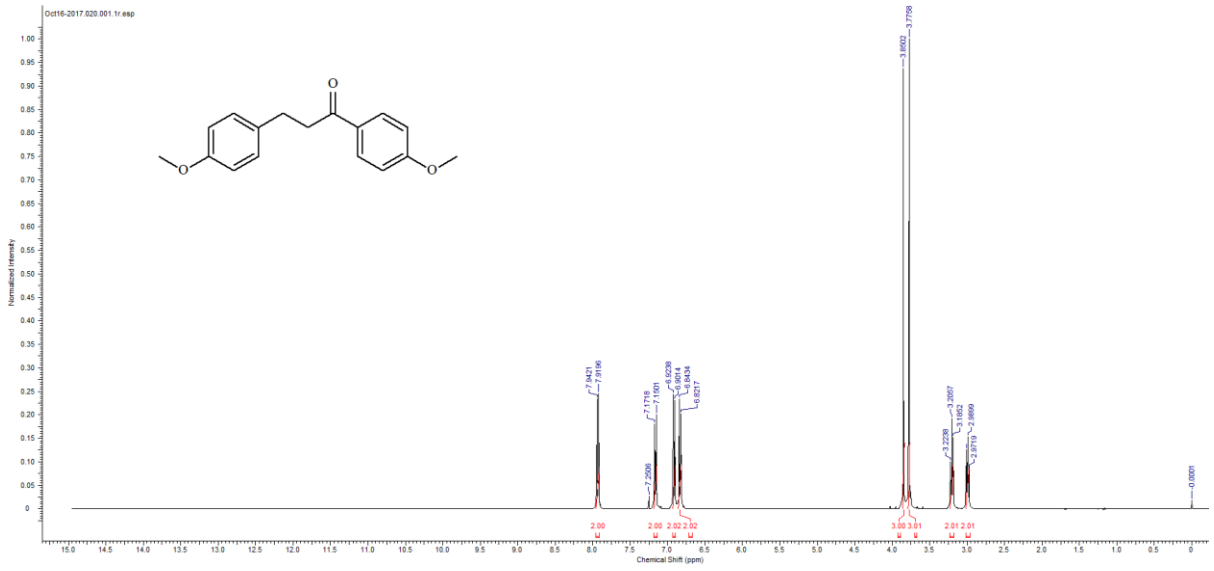
Copies of NMR spectra for the reduction of unsaturated ketones with methanol

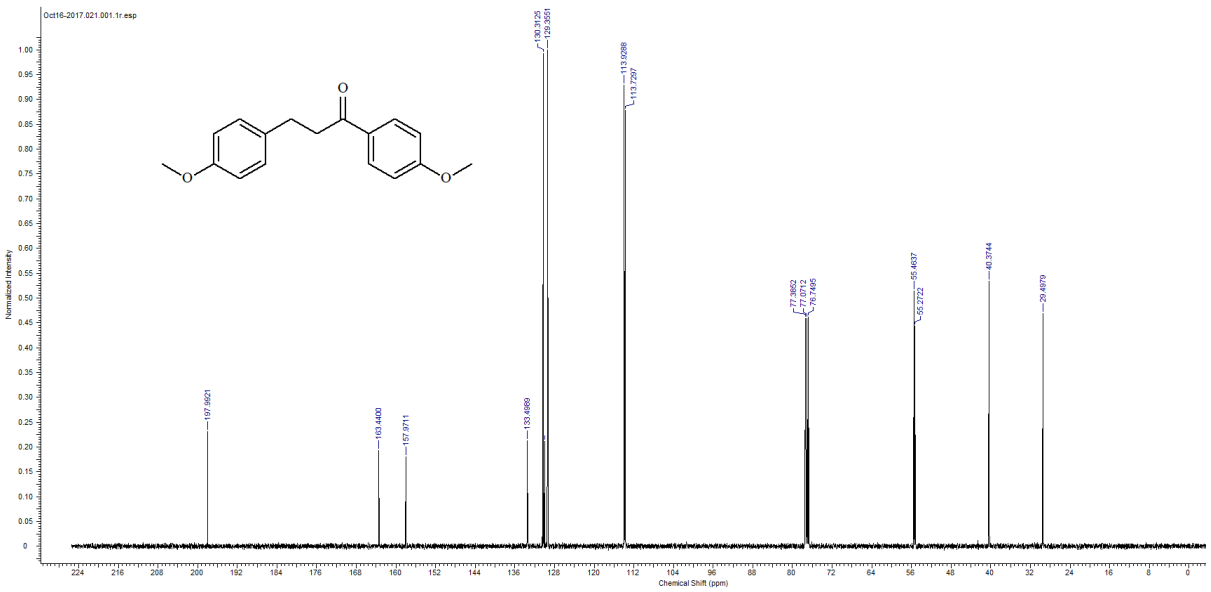




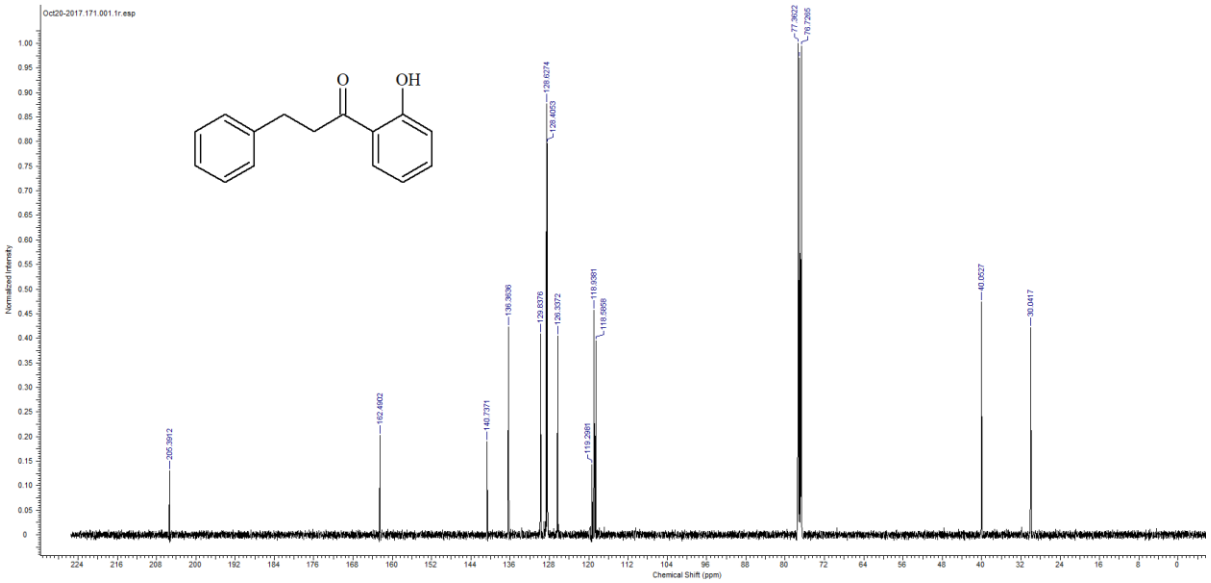

Oct16-2017.010.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
O
3.7607
7.9609
7.9423
7.5471
7.4442
7.4307
7.4256
7.1782
7.1572
6.8495
6.8280
3.2652
3.2482
3.2035
3.0102
2.9917
0.0001
1.99
1.01
2.05
2.02
2.01
3.00
2.00
1.99

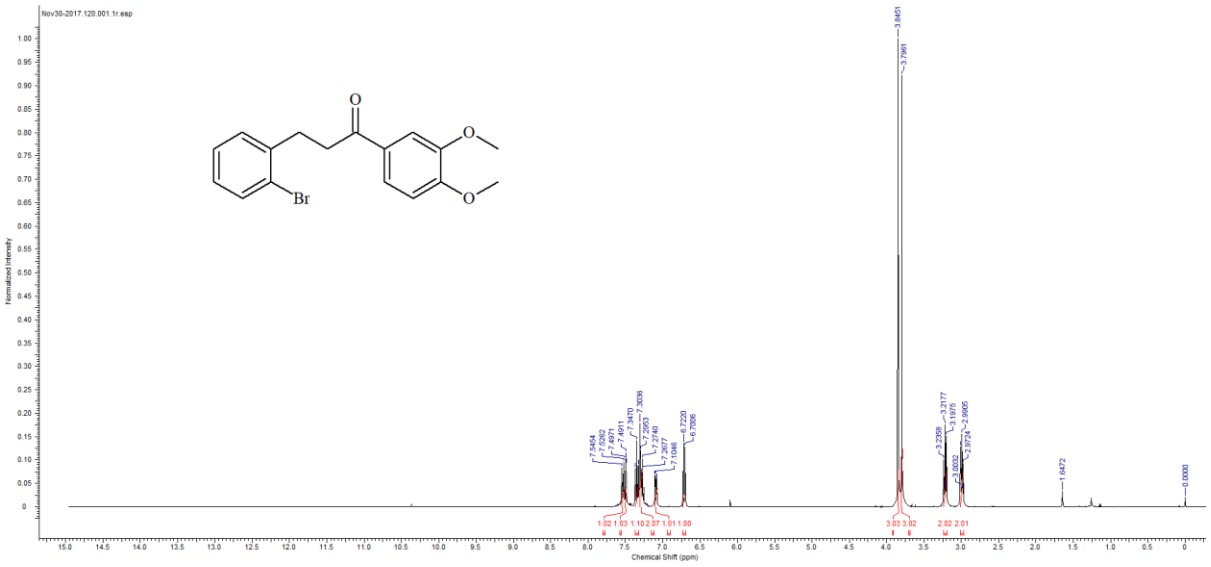

Oct16-2017.011.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
O
199.4814
159.0094
136.0227
133.3304
133.0303
129.3627
128.6045
128.0530
113.9594
77.3699
77.0482
76.7342
55.2915
40.7191
29.2867

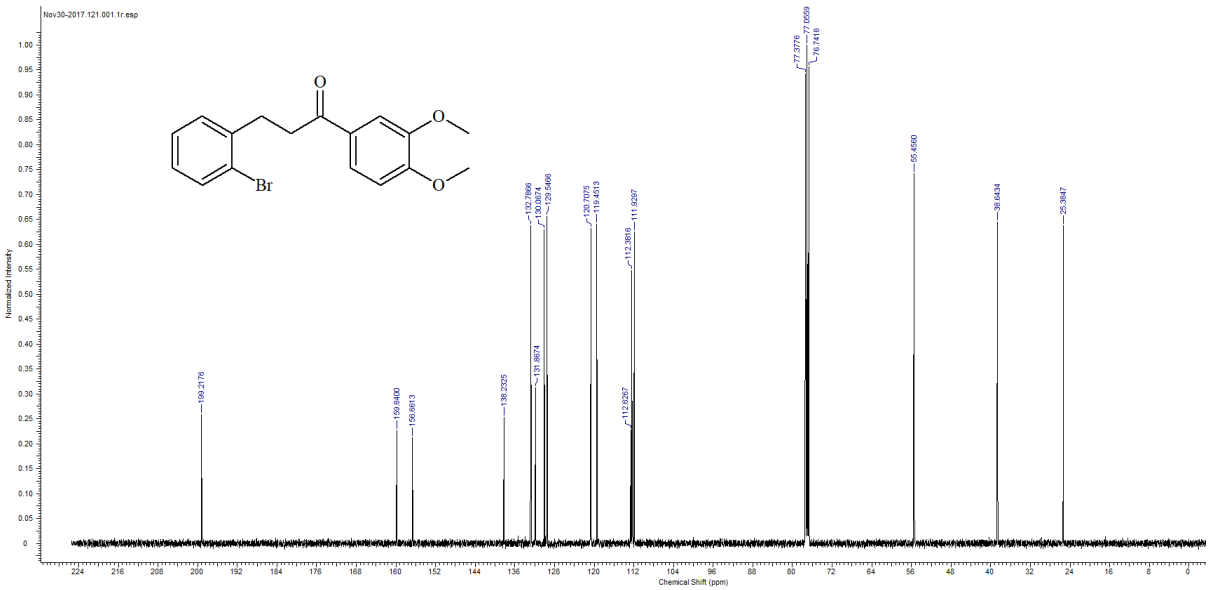

Oct16-2017.020.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
O
O
3.7758
3.6932
7.9421
7.9196
7.7178
7.7001
7.6238
7.6014
7.5434
7.5217
7.2509
3.2258
3.2057
3.1953
3.0899
2.8719
0.0001
2.00
2.00
2.02
2.02
3.00
3.01
2.01
2.01

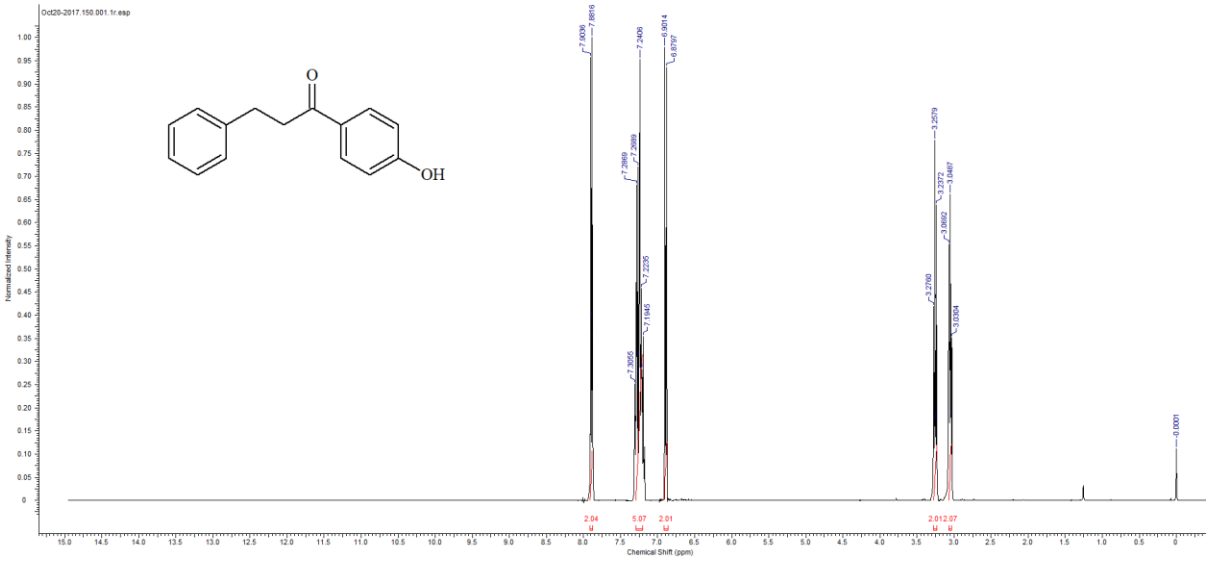

Oct16-2017.021.001.1r.esp
O
O
O
197.6921
163.4400
157.9711
133.4689
130.3126
129.3551
113.9288
113.7297
77.3652
77.0522
76.7495
55.4637
55.2722
40.3744
29.4979
Normalized Intensity
Chemical Shift (ppm)

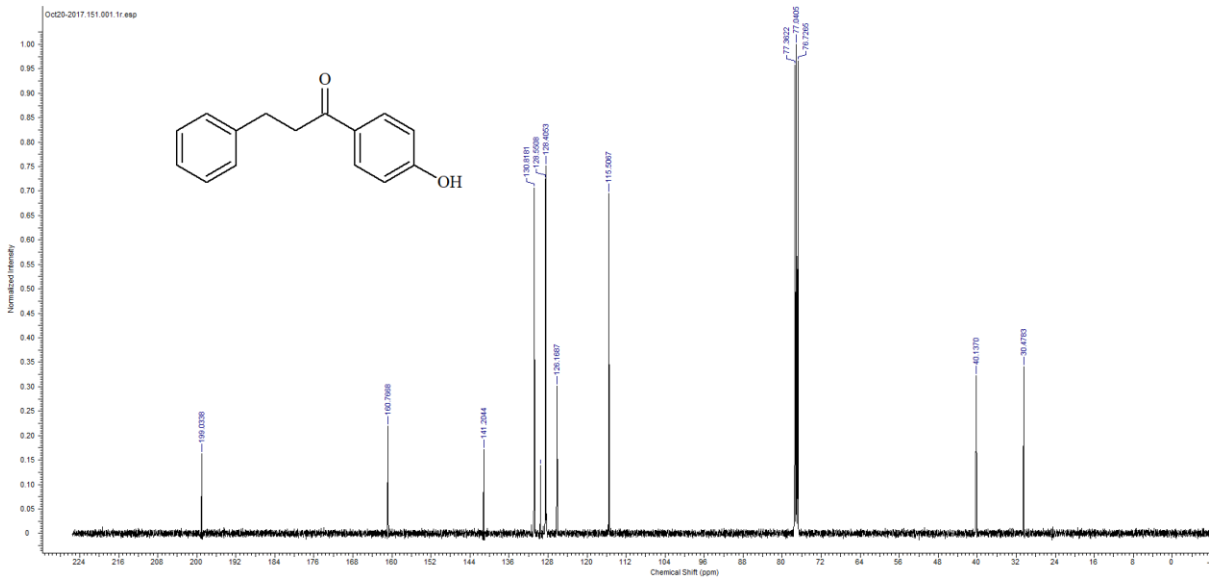

Oct20-2017.170.001.1r.esp
O
OH
12.2954
7.7498
7.7459
7.7298
7.4845
7.4759
7.3180
7.2950
7.2862
7.2372
7.1982
6.9912
6.9724
6.9710
6.8532
3.3267
3.3065
3.0858
3.0659
3.3450
3.0476
1.5714
0.0000
1.03
1.03 1.06 2.00 3.04 1.04 1.96
2.08 2.08
Normalized Intensity
Chemical Shift (ppm)

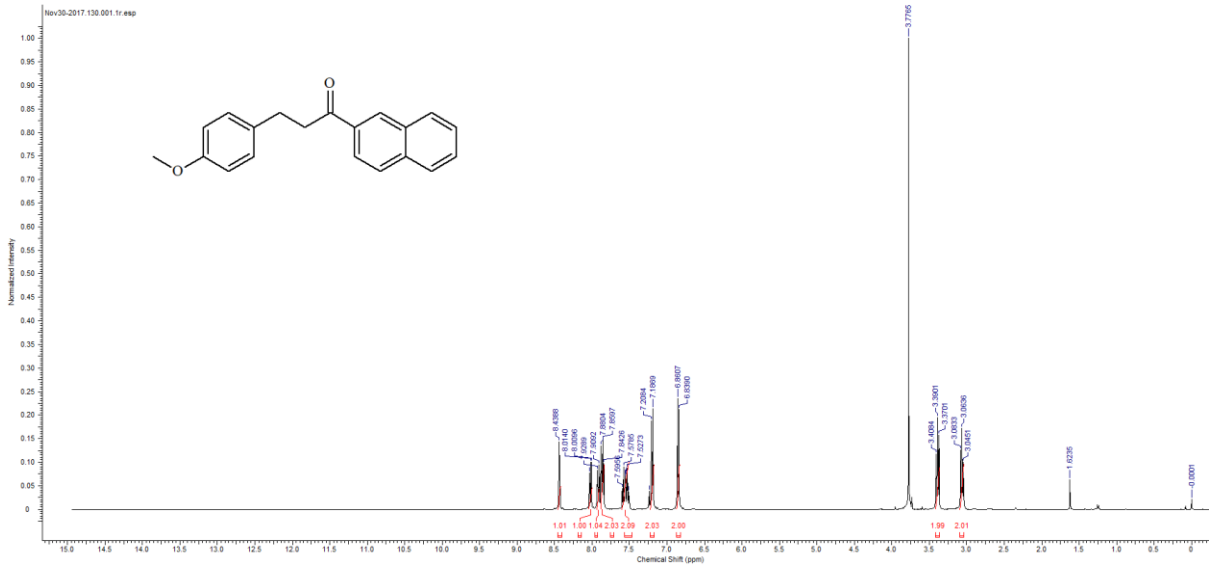

Oct20-2017.171.001.1r.esp
O
OH
205.3912
162.4902
140.7371
136.3636
129.6376
129.6274
128.4053
128.3372
119.9361
118.9959
119.2981
77.3622
76.7265
40.0527
30.0417
Normalized Intensity
Chemical Shift (ppm)

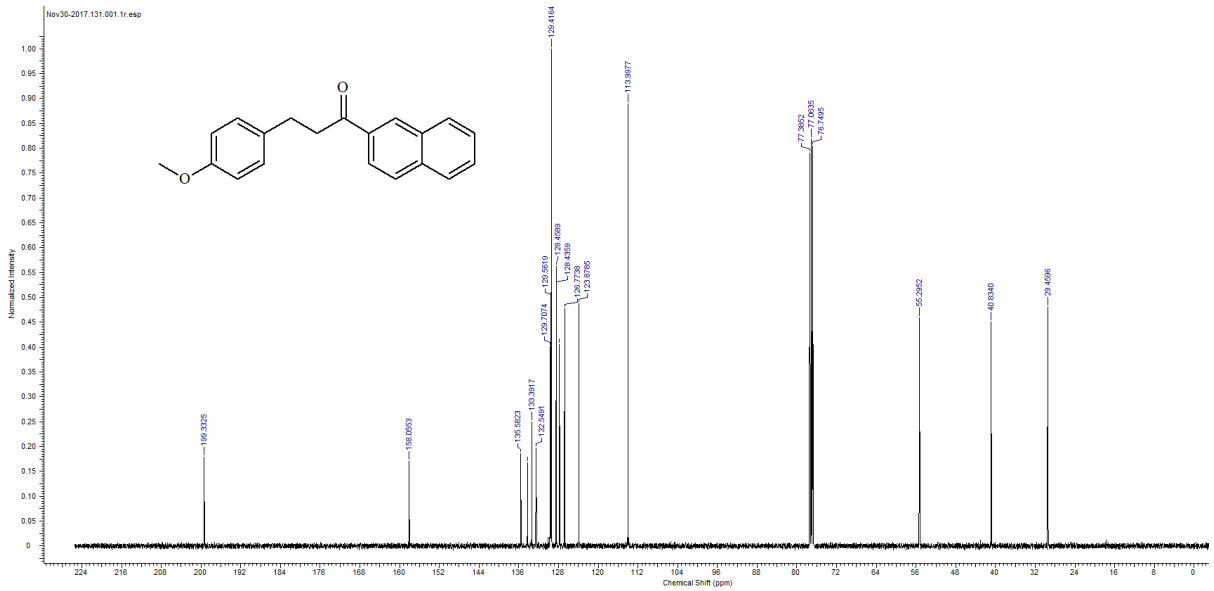

Nov30-2017.120.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
Br
O
O
O
3.8451
3.7961
7.5454
7.5302
7.4970
7.4811
7.3470
7.3036
7.2953
7.2740
7.2657
7.1048
6.7220
6.7066
3.2177
3.1975
3.0724
3.0532
3.2358
2.9605
1.6472
0.0000
1.02 1.03 1.10 2.07 1.01 1.00
3.03 3.02
2.02 2.01

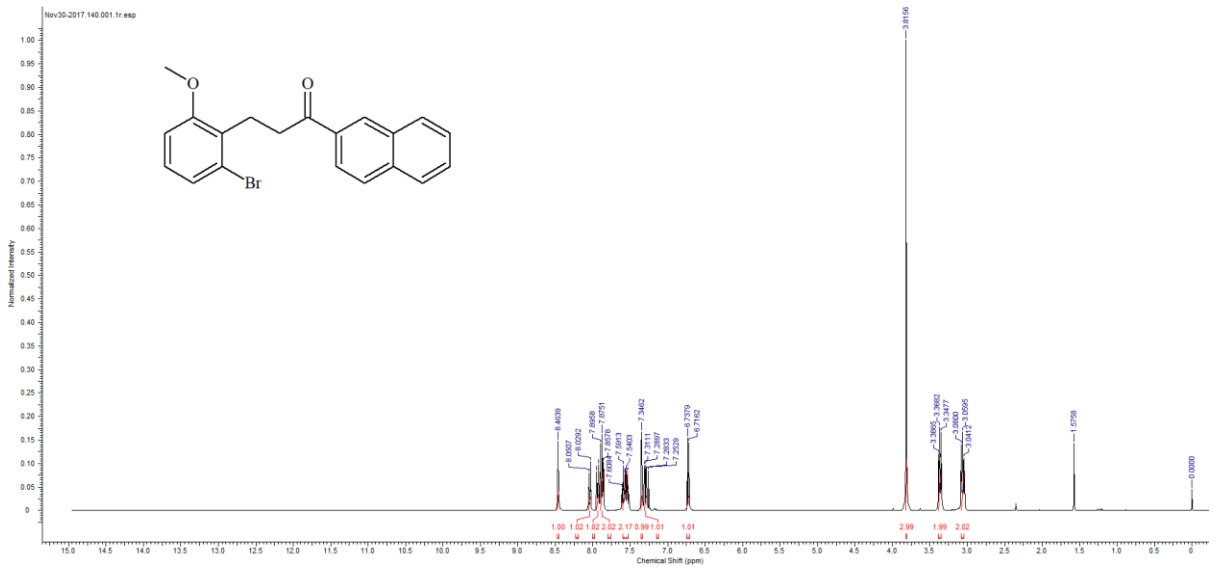

Nov30-2017.121.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
Br
O
O
O
77.3776
77.0559
76.7416
55.4560
39.6434
25.3847
132.7869
130.3574
129.5469
120.7075
119.4913
111.9267
112.9816
199.2176
159.8400
155.8613
138.2325
135.9874
112.8287


Oct20-2017.150.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
OH
O
7.8039
7.8816
7.7406
7.6914
7.6797
7.3869
7.3699
7.2235
7.1948
7.2805
3.2579
3.2372
3.0467
3.0862
3.2760
3.0384
0.0000
2.04
5.07
2.01
2.01
2.07


Oct20-2017.151.001.1r.esp
O
OH
Normalized Intensity
Chemical Shift (ppm)
199.0338
160.7668
141.2644
130.8191
129.5008
126.4653
126.1697
115.5097
77.3822
77.0405
76.7268
65.1370
30.4763


Nov30-2017.130.001.1r.esp
O
O
Normalized Intensity
Chemical Shift (ppm)
8.4386
8.0140
8.0096
7.9959
7.8852
7.8804
7.8697
7.8429
7.5765
7.5273
7.2084
7.1669
6.8907
6.8390
3.7765
3.4484
3.3801
3.3701
3.0063
3.0451
3.0036
1.6235
-0.0001
1.01
1.00
1.00
1.04
2.03
2.09
2.03
2.00
1.99
2.01


Nov30-2017.131.001.1r.esp
O
O
Normalized Intensity
Chemical Shift (ppm)
198.3325
158.0053
135.5823
133.3917
132.5481
129.7074
129.5819
129.4164
128.4589
128.4484
126.7738
123.8765
113.9877
77.3822
77.0535
76.7495
55.2952
40.8340
29.4596


Nov30-2017.140.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
O
Br
8.4639
8.0257
8.0242
7.8958
7.8751
7.8570
7.8513
7.8493
7.7403
7.3462
7.2511
7.2397
7.2353
7.2329
6.7379
6.7162
3.8156
3.3952
3.3677
3.0800
3.0547
3.0595
1.5758
0.0000
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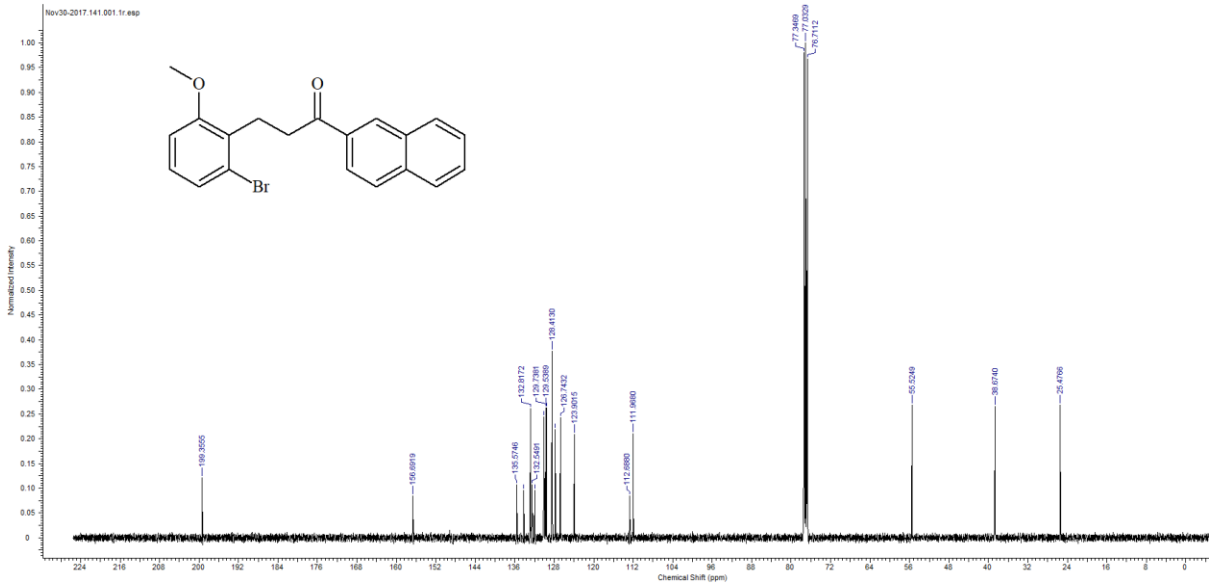
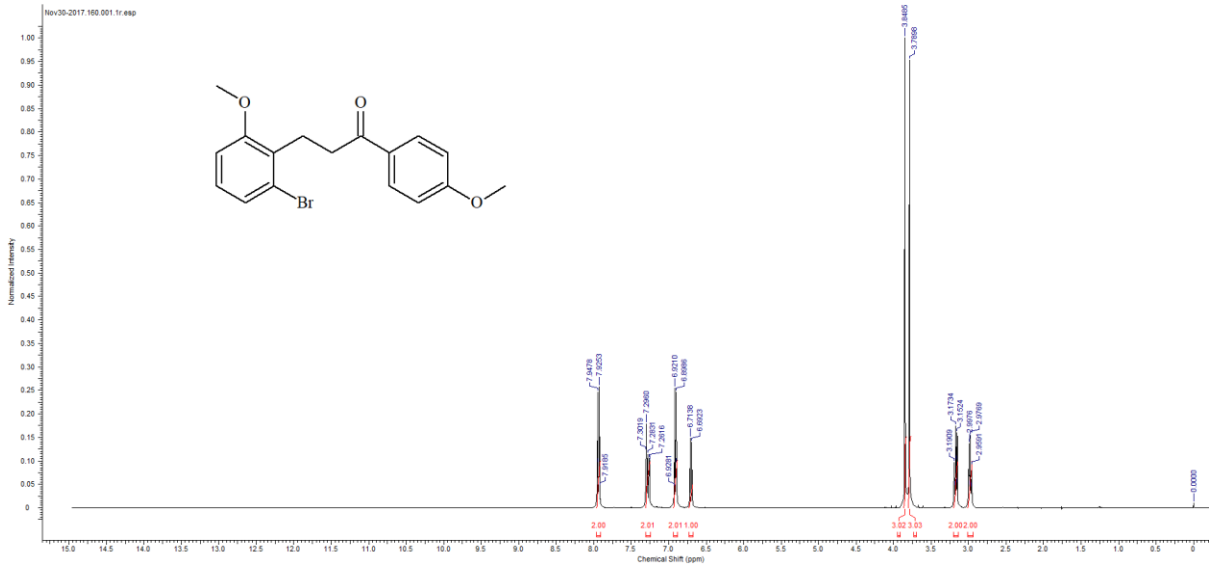
2.99 1.99 2.02


Nov30-2017.141.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
O
Br
77.3499
77.0339
76.7112
199.2655
156.6919
135.5746
132.8172
132.5491
129.7381
129.5389
128.4130
126.7432
123.9015
112.8880
111.9080
55.5249
38.6740
25.4706


Nov30-2017.160.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
O
Br
O
7.9478
7.9253
7.9186
7.3019
7.2960
7.2870
7.2816
7.2601
6.9210
6.8986
6.7138
6.6923
3.8465
3.7886
3.1904
3.1734
3.1534
2.9975
2.9691
2.9769
0.0000
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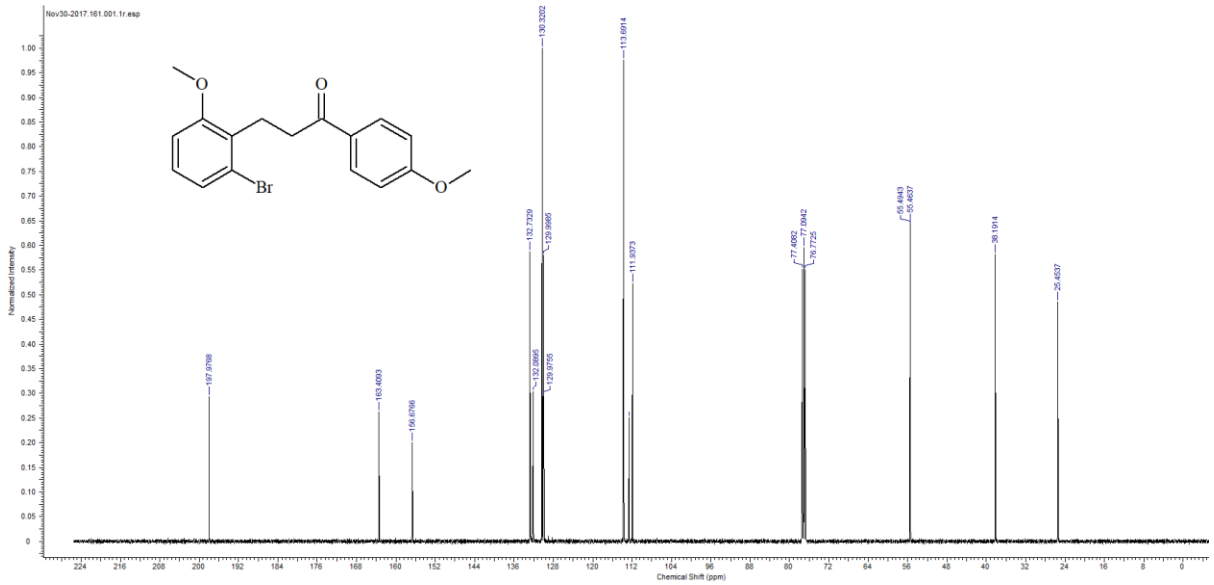
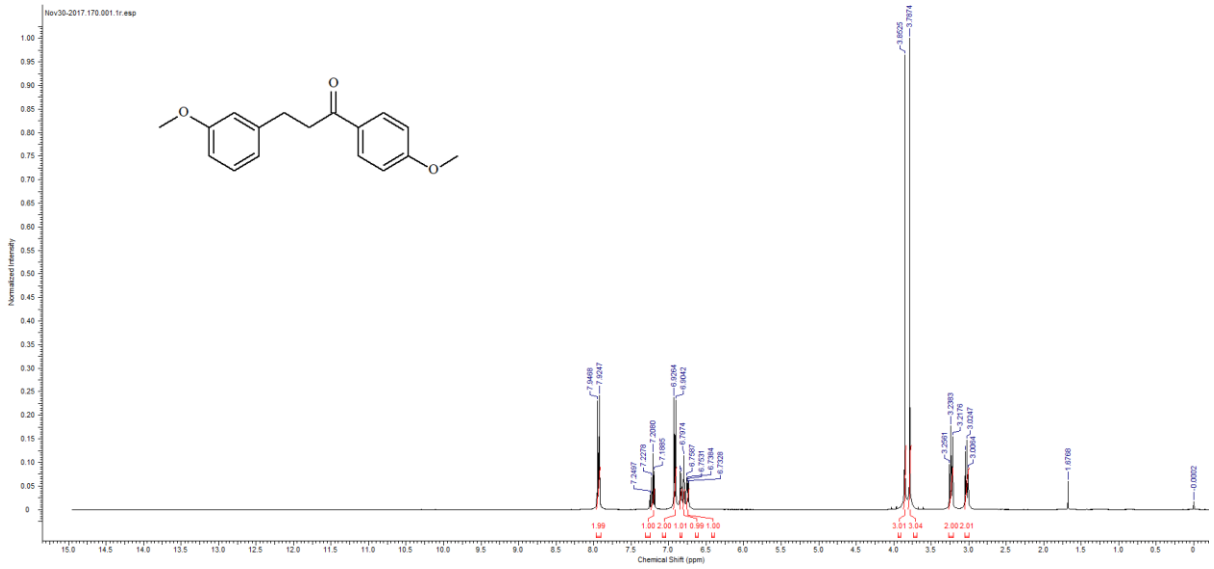
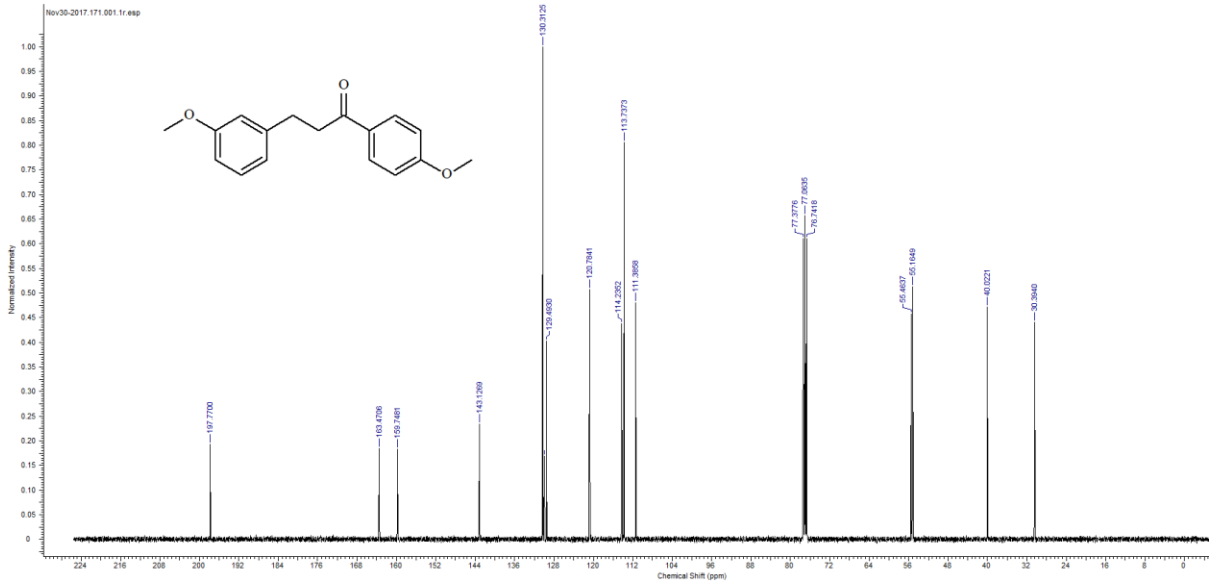
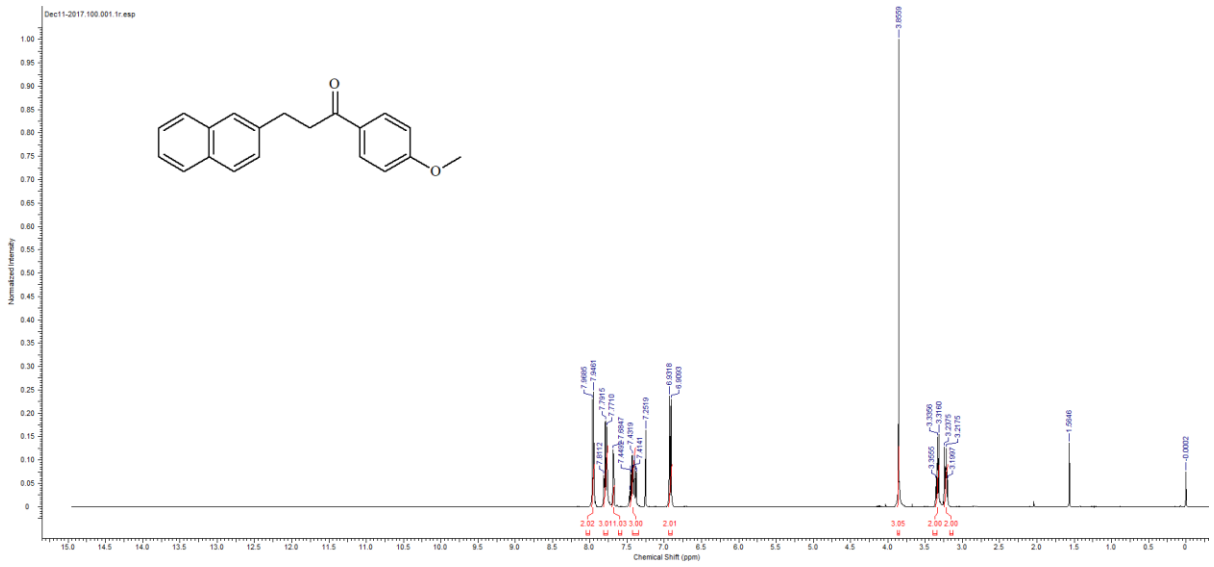
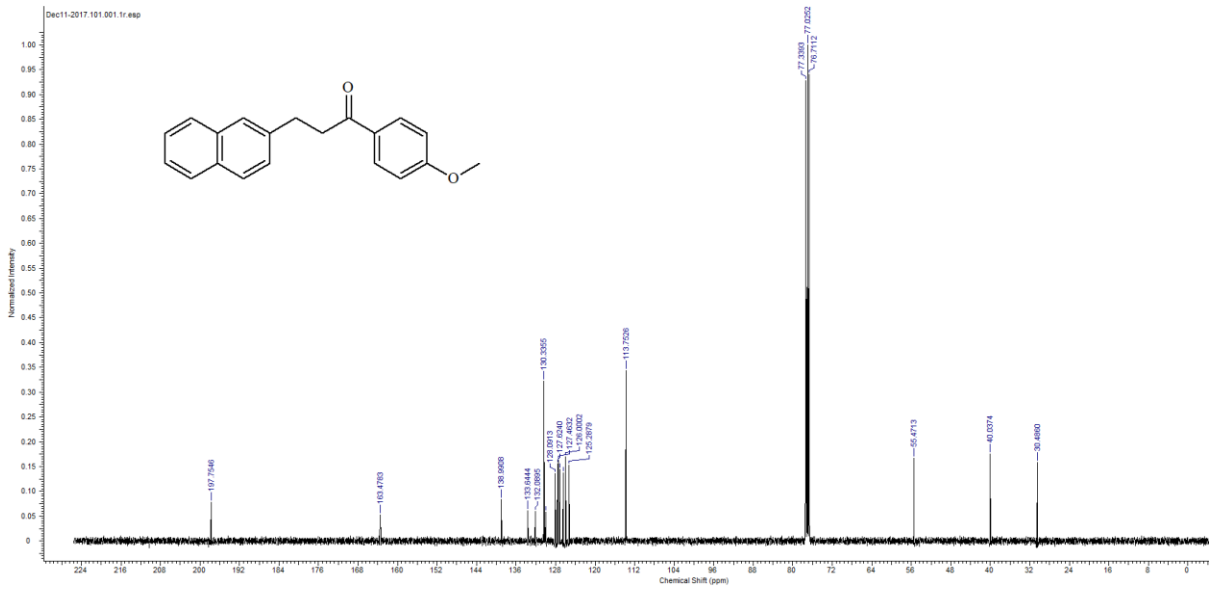
3.02 3.03 2.00 2.00


Nov30-2017.161.001.1r.esp
Br
O
O
O
197.9788
163.4093
156.6766
132.7329
132.0895
129.9755
130.3202
129.9985
113.6914
111.9373
77.4092
77.0942
76.7725
55.6943
55.4637
38.1914
25.4537
Normalized Intensity
Chemical Shift (ppm)

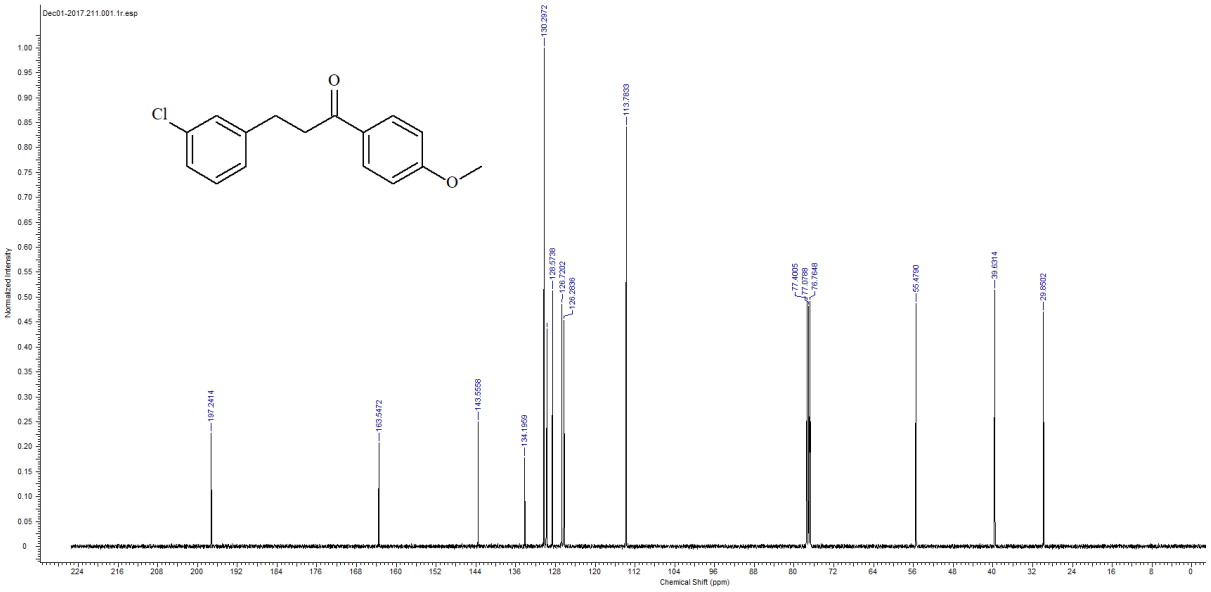

Nov30-2017.170.001.1r.esp
O
O
O
3.8525
3.7874
7.9468
7.9247
7.2278
7.2060
7.1885
6.9364
6.9042
6.7974
6.7569
6.7031
6.7384
6.7038
3.2581
3.2383
3.2276
3.0247
3.0064
1.6766
0.0002
1.99
1.00
2.00
1.00
1.01
0.99
1.00
3.01
3.04
2.00
2.01
Normalized Intensity
Chemical Shift (ppm)

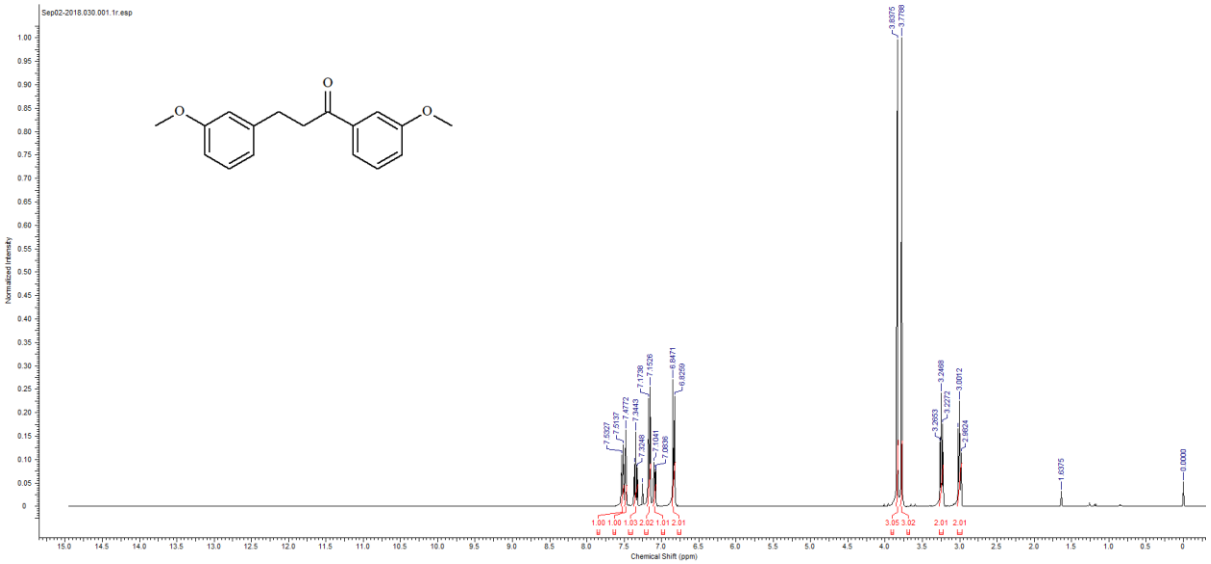

Nov30-2017.171.001.1r.esp
O
O
O
197.7700
163.4706
159.7481
143.1269
130.3125
129.4690
120.7841
114.2952
113.7373
111.3898
77.3776
77.0635
76.7418
55.4637
55.1649
40.0221
30.3940
Normalized Intensity
Chemical Shift (ppm)


Dec11-2017.100.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)


Dec11-2017.101.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)


Dec01-2017.210.001.1r.esp
Cl
Normalized Intensity
Chemical Shift (ppm)


Dec01-2017.211.001.1r.esp
Cl
O
O
Normalized Intensity
Chemical Shift (ppm)
197.2414
163.5472
143.5559
134.1959
130.2972
129.5726
129.1722
126.2838
113.7833
77.4008
77.0789
76.7569
55.4790
39.6314
29.6592


Sep02-2018.030.001.1r.esp
O
O
O
Normalized Intensity
Chemical Shift (ppm)
7.9327
7.9137
7.4772
7.3443
7.3246
7.1726
7.1526
7.1041
7.0836
6.8471
6.8259
3.8375
3.7766
3.2468
3.2272
3.2053
3.0872
2.8624
1.6375
0.0000
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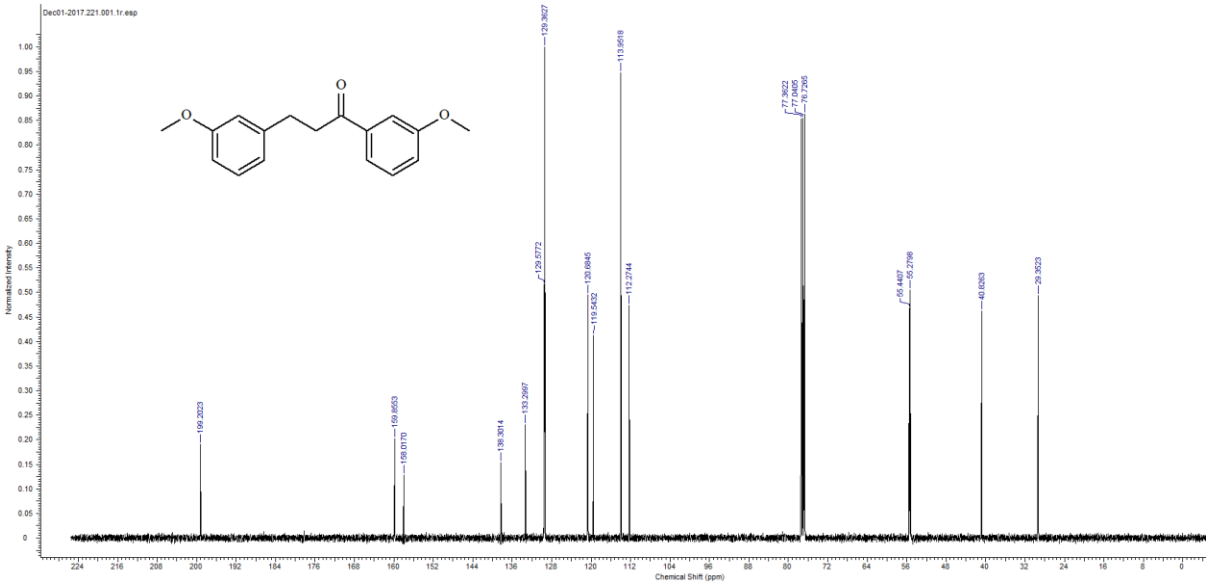
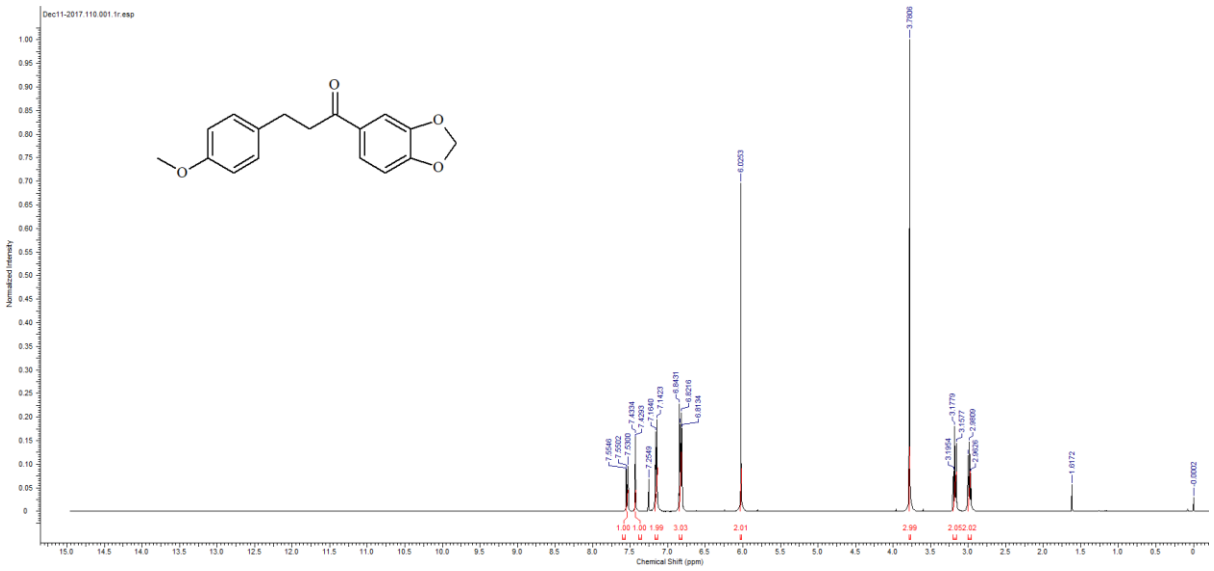
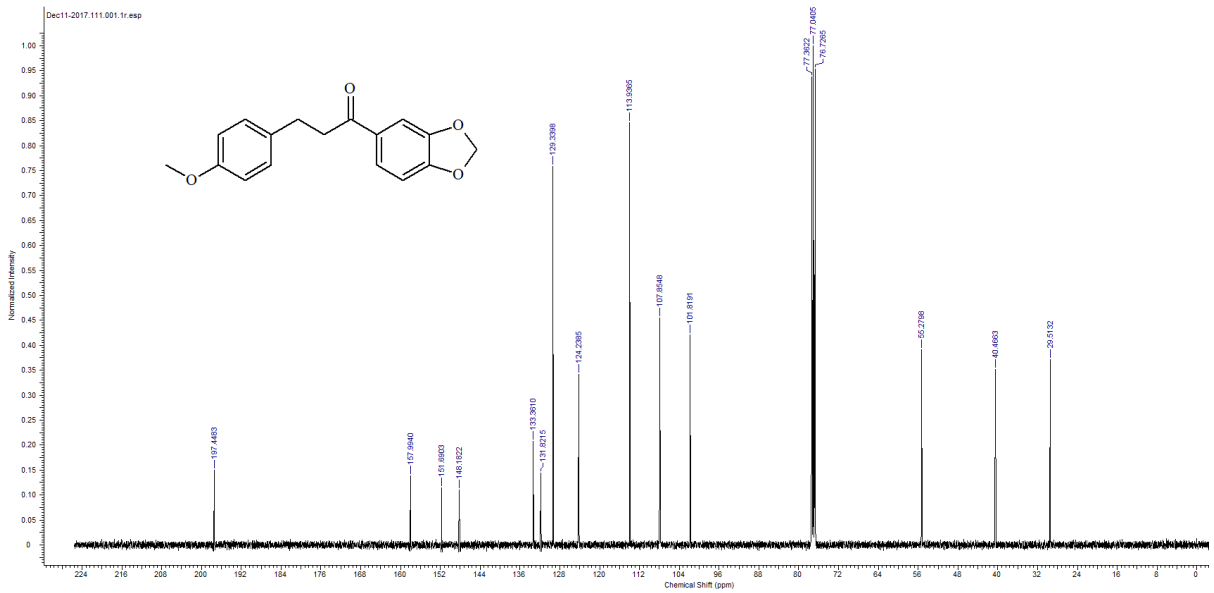
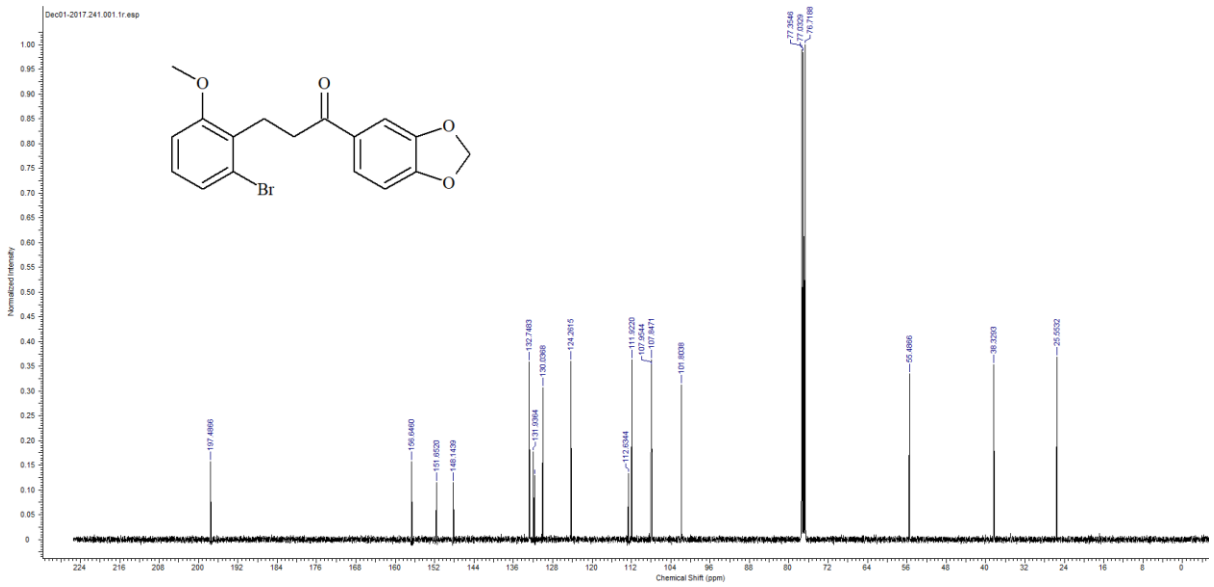
3.05 3.02
2.01 2.01


Dec01-2017.221.001.1r.esp
O
O
O
Normalized Intensity
Chemical Shift (ppm)
199.2023
159.8553
159.0170
138.3014
133.2997
129.5772
129.3627
120.6845
119.5402
113.9518
112.2744
77.3622
77.0405
76.7205
55.4487
55.2798
49.8263
29.3523

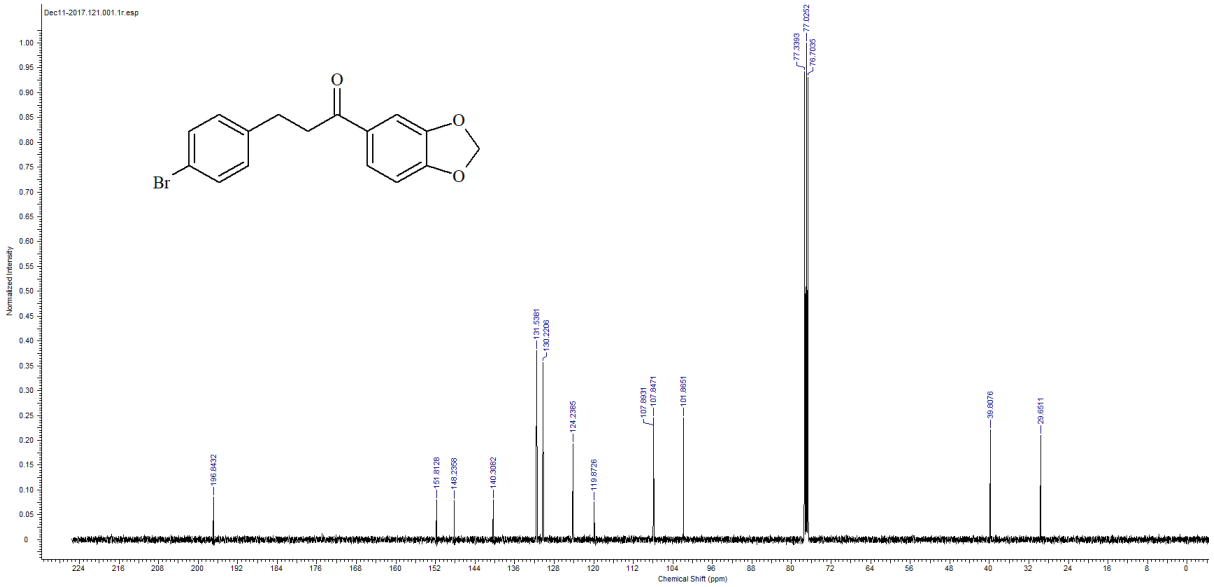

Dec11-2017.110.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
O
O
O
7.5546
7.5502
7.5300
7.4334
7.4293
7.4160
7.2549
7.1423
6.8431
6.8216
6.8134
6.0253
3.7606
3.1779
3.1577
3.1464
3.0826
2.9869
1.6172
-0.0002
1.00 1.00 1.00 1.99 3.03 2.01 2.99 2.05 2.02

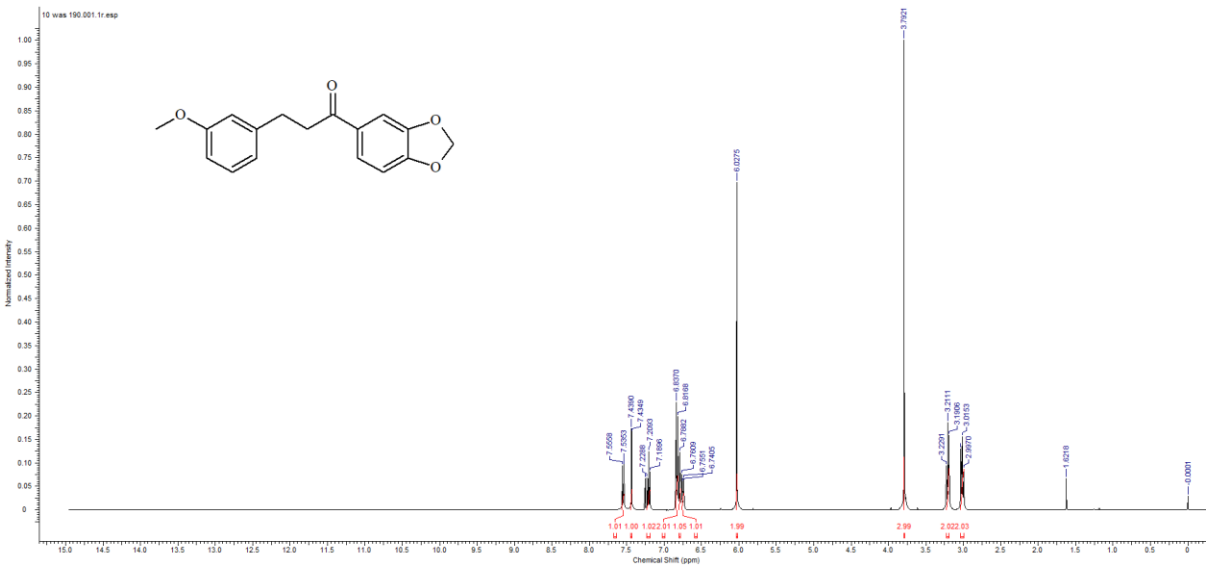

Dec11-2017.111.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
O
O
O
197.4483
157.9940
151.6903
148.1922
133.3610
131.8215
129.3398
124.2395
113.9365
107.9548
101.8191
77.3622
77.0405
76.7265
55.2798
40.4693
29.5132

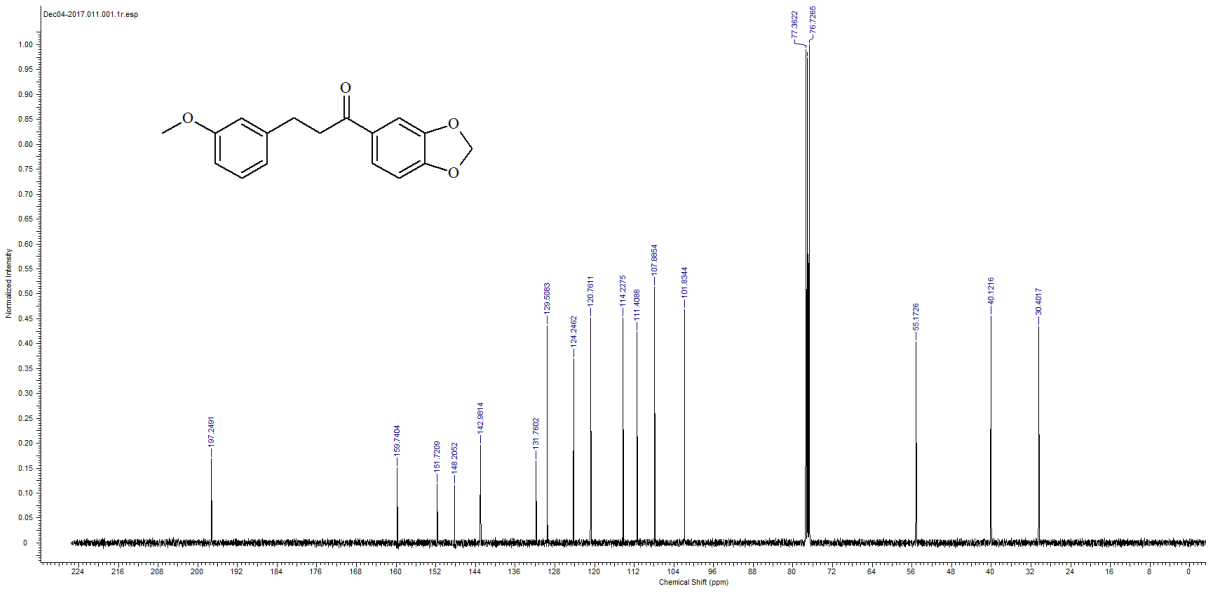

Dec01-2017.240.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
O
O
O
Br
7.4533
7.3946
7.2746
7.2697
7.2600
6.8401
6.8196
6.7927
6.7703
6.0323
3.8049
3.1468
3.1276
3.0933
2.9825
1.6141
-0.0002
1.00 1.00 2.00 1.01 1.00 2.03 3.02 2.01 1.99

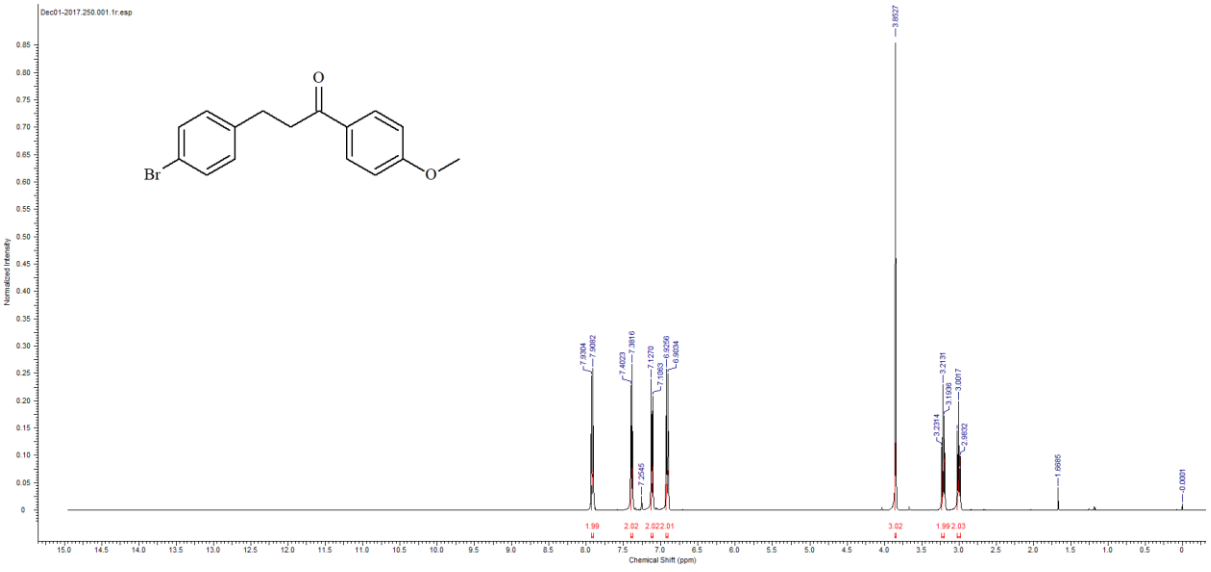

Dec01-2017.241.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
O
O
O
Br

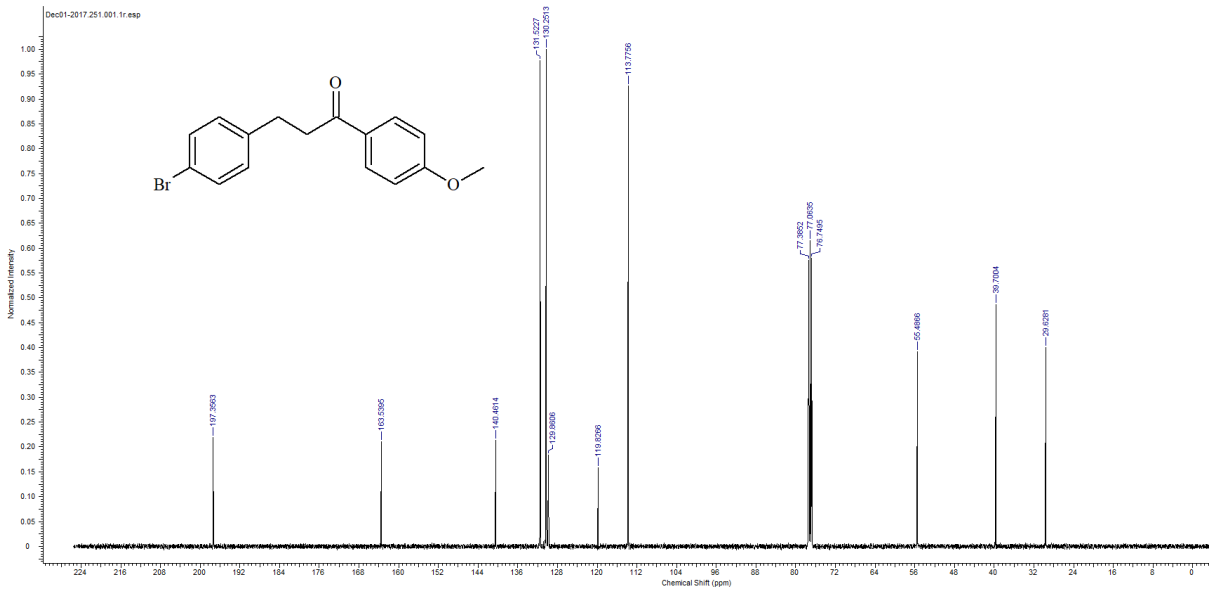

Dec11-2017.120.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
O
O
Br

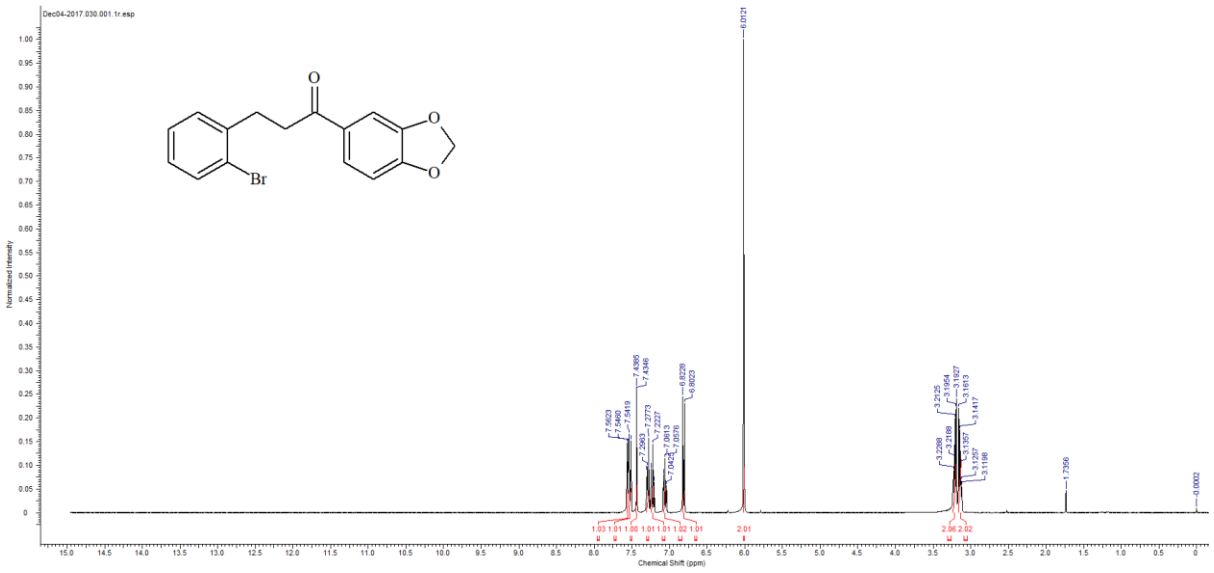

Dec11-2017.121.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
O
O
Br


10 was 190.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
3.7921
6.0275
7.5559
7.5353
7.4390
7.4349
7.2886
7.2693
7.1896
6.8370
6.8168
6.7892
6.7709
6.7551
6.7405
3.2291
3.2111
3.1936
3.1763
3.0153
2.9970
1.6218
0.0001
1.01 1.00 1.02 2.01 1.05 1.01
1.99
2.99
2.022.03

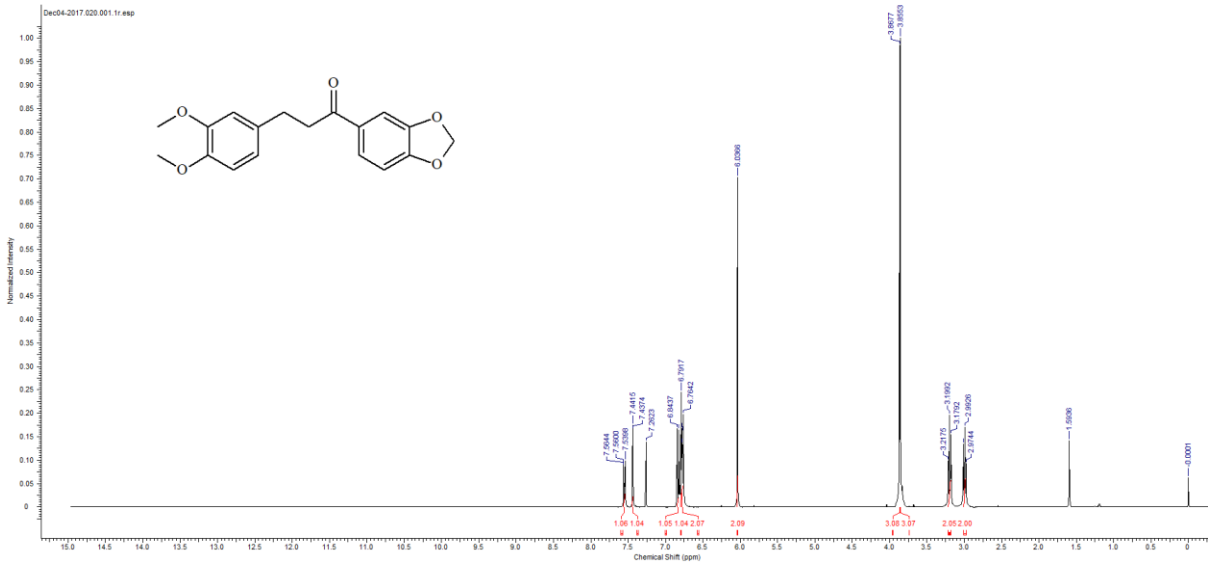

Dec04-2017.011.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
77.3622
76.7265
197.2491
159.7404
151.7209
148.2052
142.9814
131.7602
129.5083
124.2462
120.7911
114.2275
111.4086
107.6854
101.6344
55.1726
40.1216
30.4017

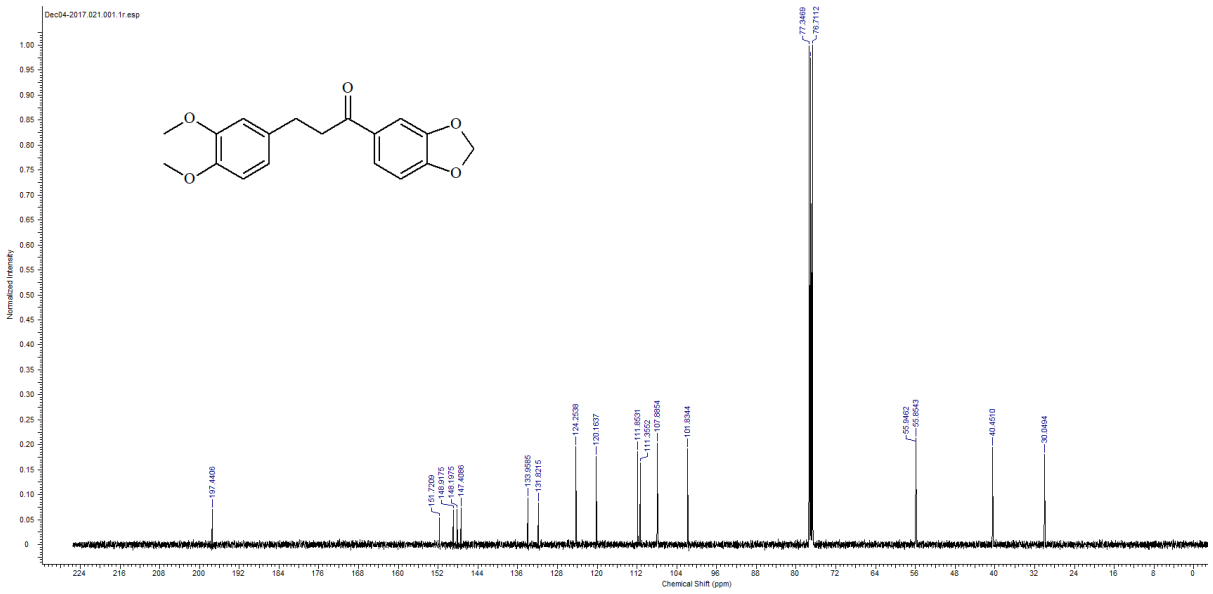

Dec01-2017.250.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
3.8927
7.9304
7.9062
7.4023
7.3816
7.1370
7.1063
6.8256
6.8064
3.2914
3.2131
3.1936
3.0071
2.9802
1.6665
0.0001
1.99
2.02
2.022.01
3.02
1.99 2.03

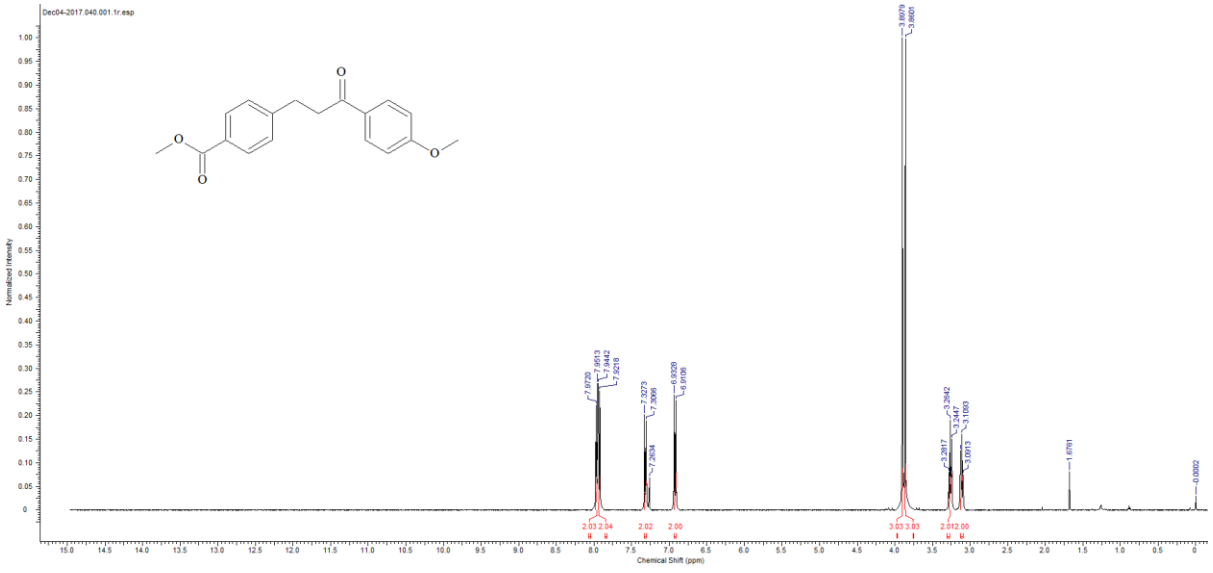

Dec01-2017.251.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
Br
O
197.3563
163.5395
140.4614
131.5227
130.2513
129.8606
119.8266
113.7759
77.3852
77.0635
76.7418
55.4866
39.7004
29.6281

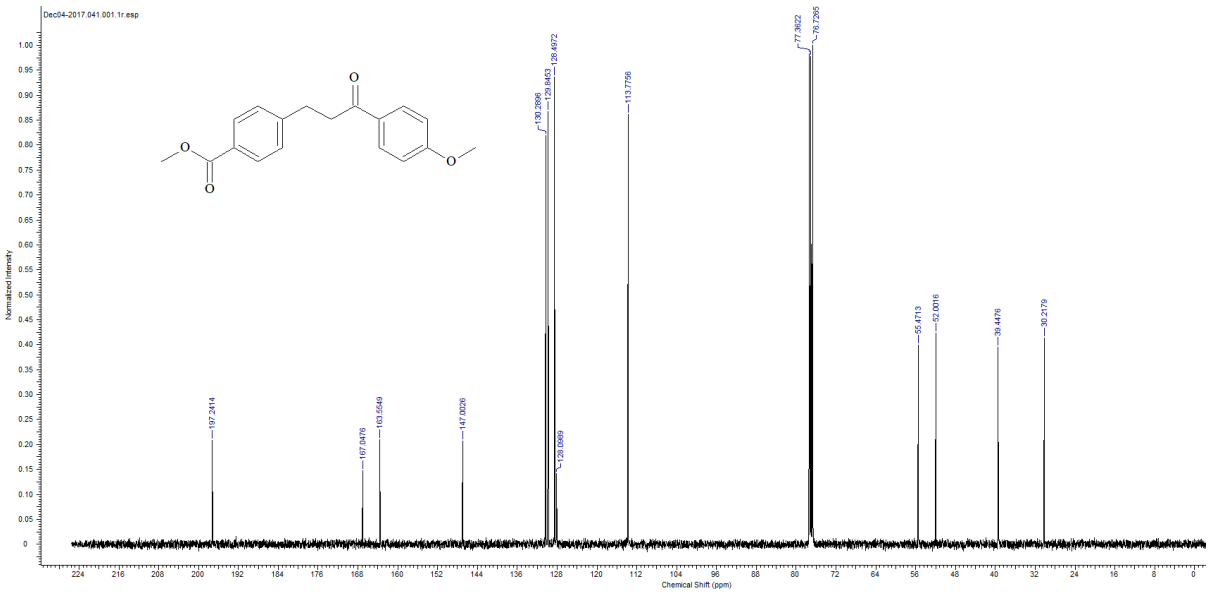

Dec04-2017.030.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
Br
O
O
6.0121
7.8623
7.5460
7.5419
7.4386
7.4346
7.3773
7.2227
7.1939
7.1878
7.0424
6.8239
6.8023
3.2125
3.2064
3.1927
3.1613
3.1417
3.2288
3.2188
3.1357
3.1287
3.1198
1.7356
0.0002
1.03 1.01 1.00 1.01 1.01 1.02 1.01
2.01
2.06 2.02

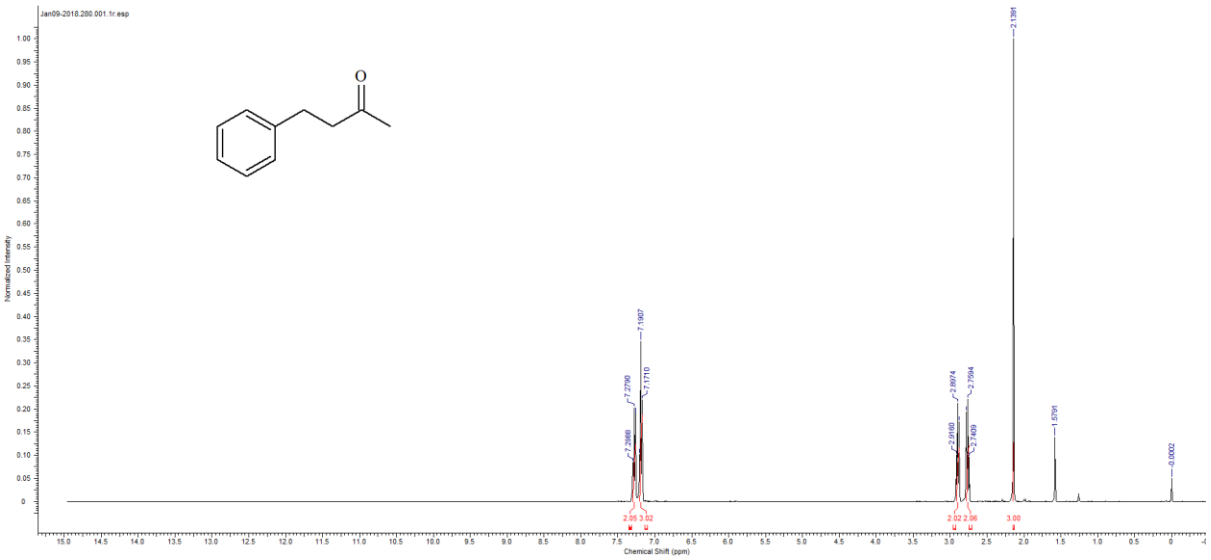

Dec04-2017.031.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
Br
O
O
196.9657
151.7669
148.1975
140.6146
132.8785
130.7674
127.9764
127.6394
124.3304
107.8654
101.8574
77.4159
76.7801
39.3753
31.8298


Dec04-2017.020.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)

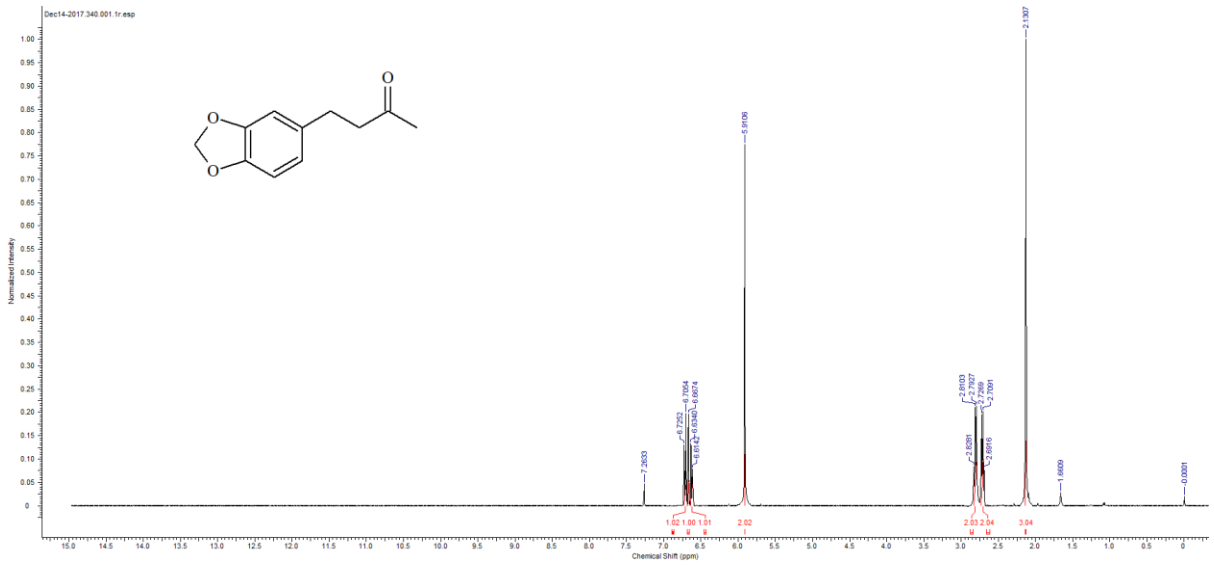

Dec04-2017.021.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)

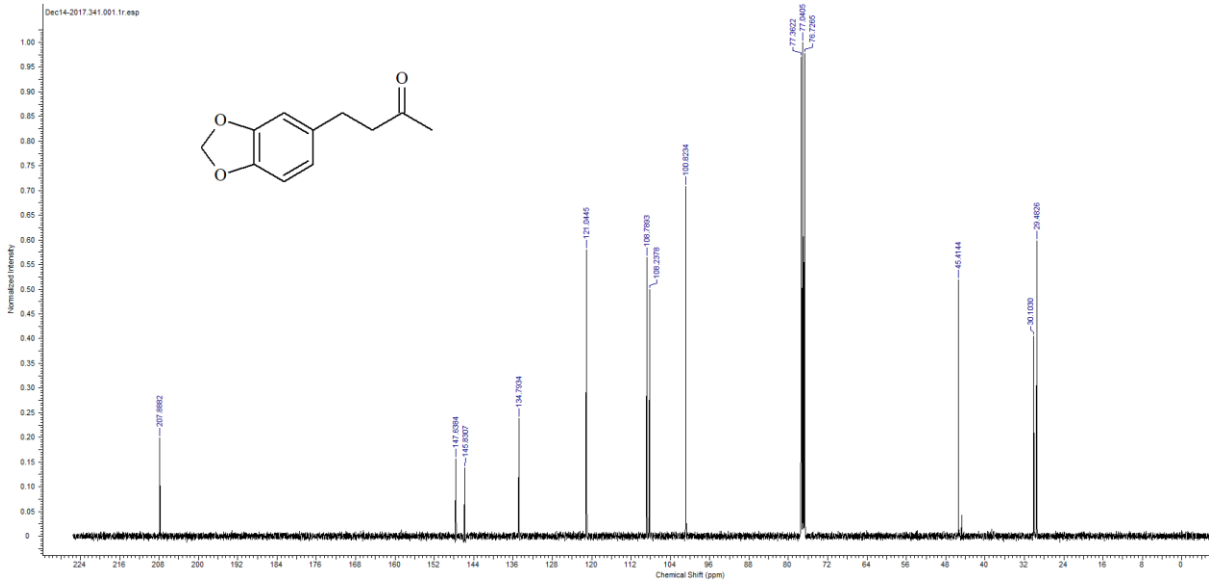

Dec04-2017.040.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)

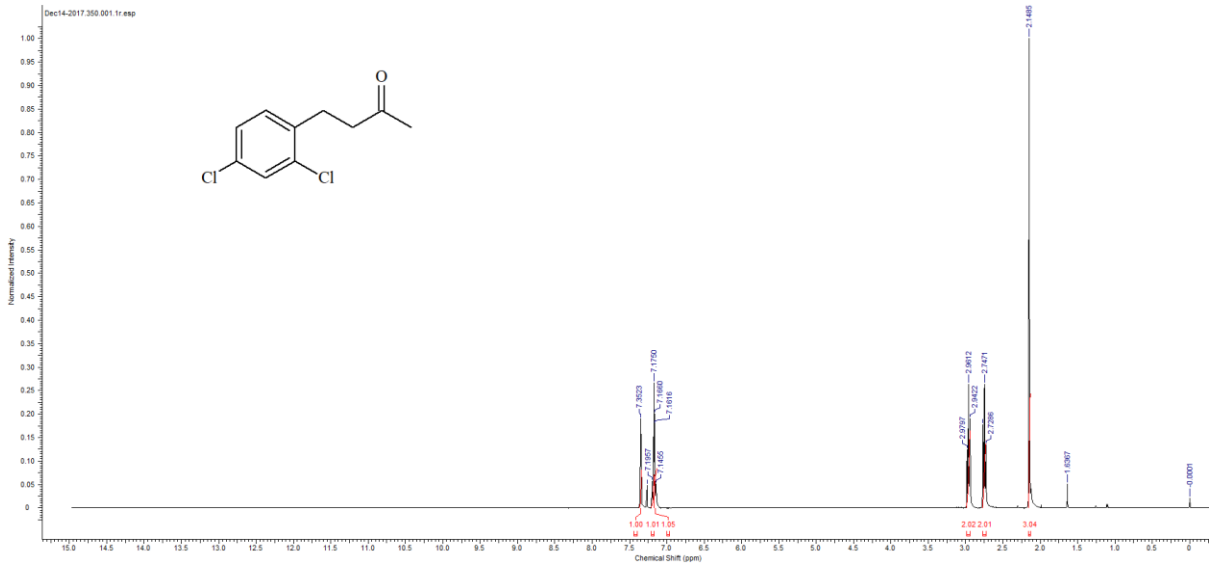

Dec04-2017.041.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
197.2414
167.0476
163.5549
147.0026
130.2898
129.8453
126.4972
126.0869
113.7756
77.3622
77.0000
76.7295
55.4713
52.0016
39.4476
30.2179

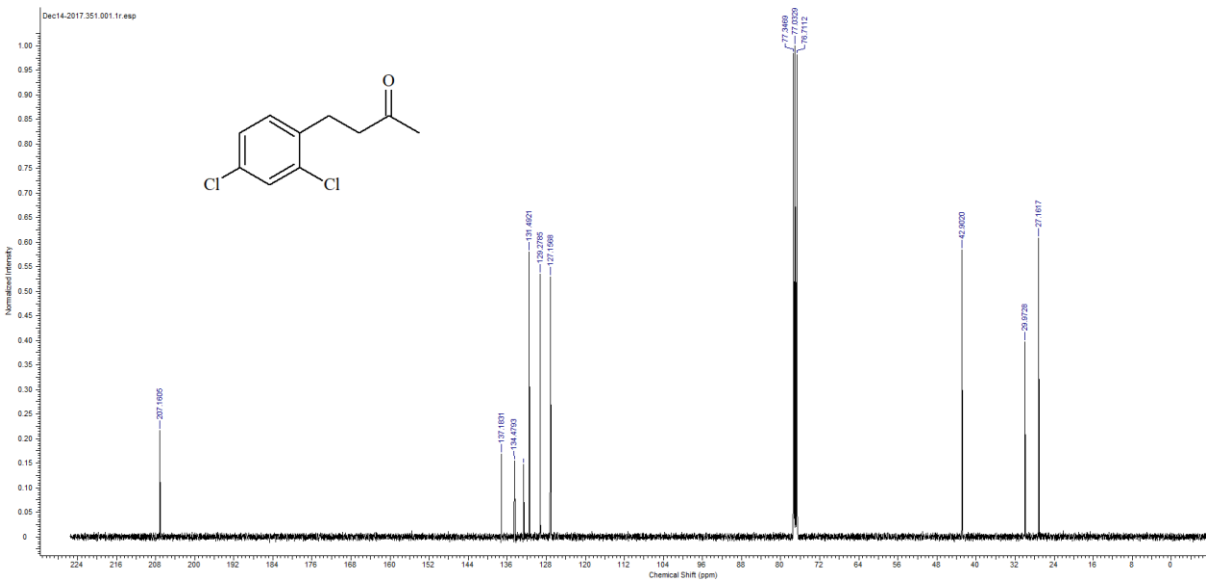

Jan09-2018.280.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
7.2868
7.2790
7.1710
7.1907
2.9460
2.8974
2.7594
2.7409
2.1391
1.5791
0.0002
2.05 3.02
2.02 2.06
3.00

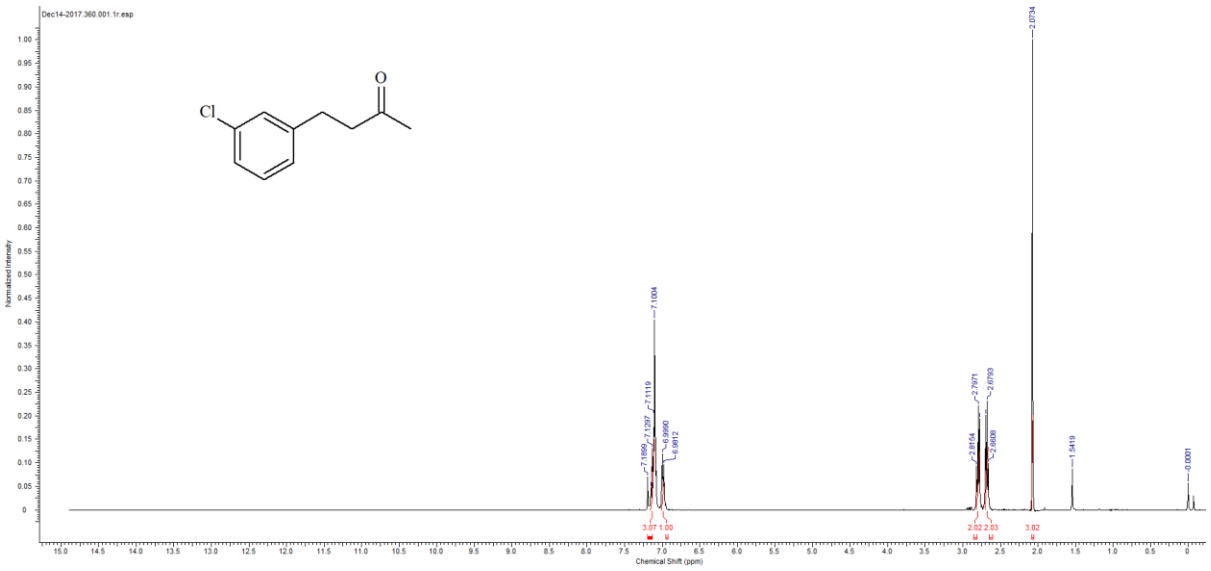

Jan09-2018.281.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
207.9265
140.9976
126.5049
126.2904
126.1151
77.3393
77.0000
76.7035
45.1846
30.0723
29.7438


Dec14-2017.340.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
O
O
7.2633
6.7252
6.7054
6.6974
6.6742
6.6358
6.6074
5.9106
2.9933
2.7927
2.7289
2.7091
2.6291
2.5916
2.1307
1.6809
0.0001
1.02 1.00 1.01
2.02
2.03 2.04
3.04

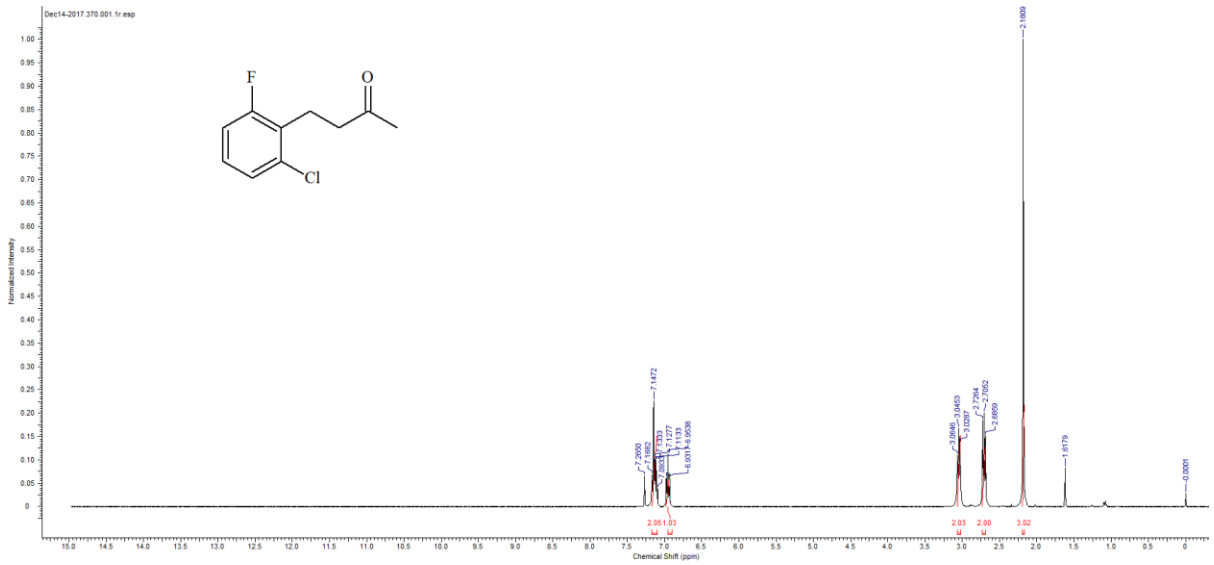

Dec14-2017.341.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
O
O
207.8892
147.6394
146.8307
134.7934
121.0445
108.7893
108.2379
100.8234
77.3622
77.0405
76.7265
65.4144
30.1030
29.4826

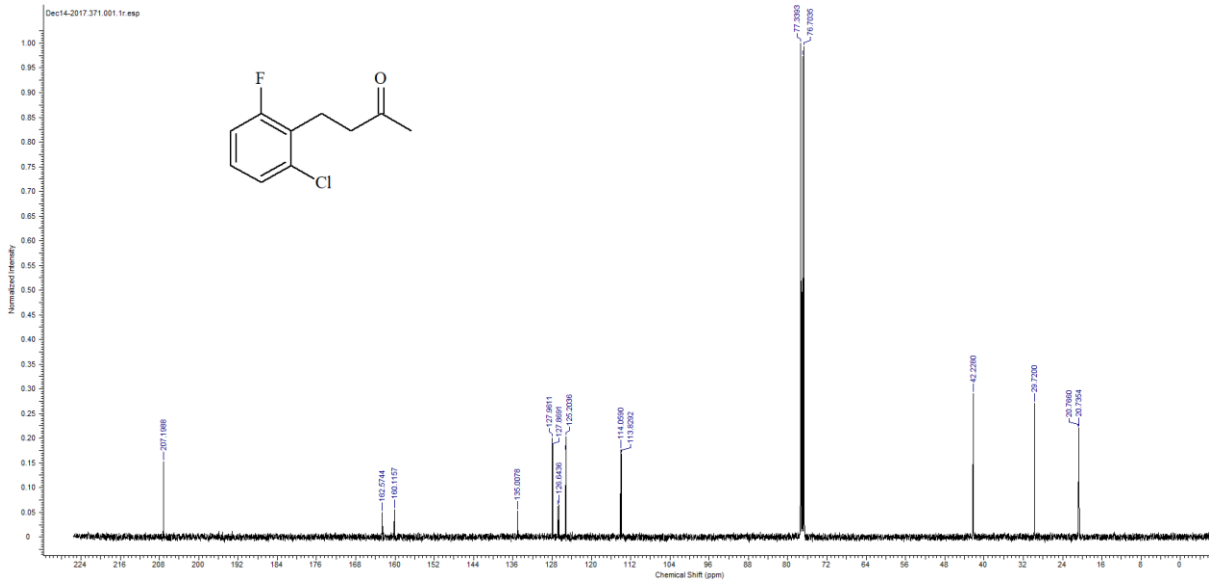

Dec14-2017.350.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
Cl
Cl
7.3523
7.1967
7.1760
7.1660
7.1616
7.1455
2.9707
2.9612
2.9422
2.7386
2.1471
2.1465
1.8367
0.0001
1.00 1.01 1.05
2.02 2.01
3.04

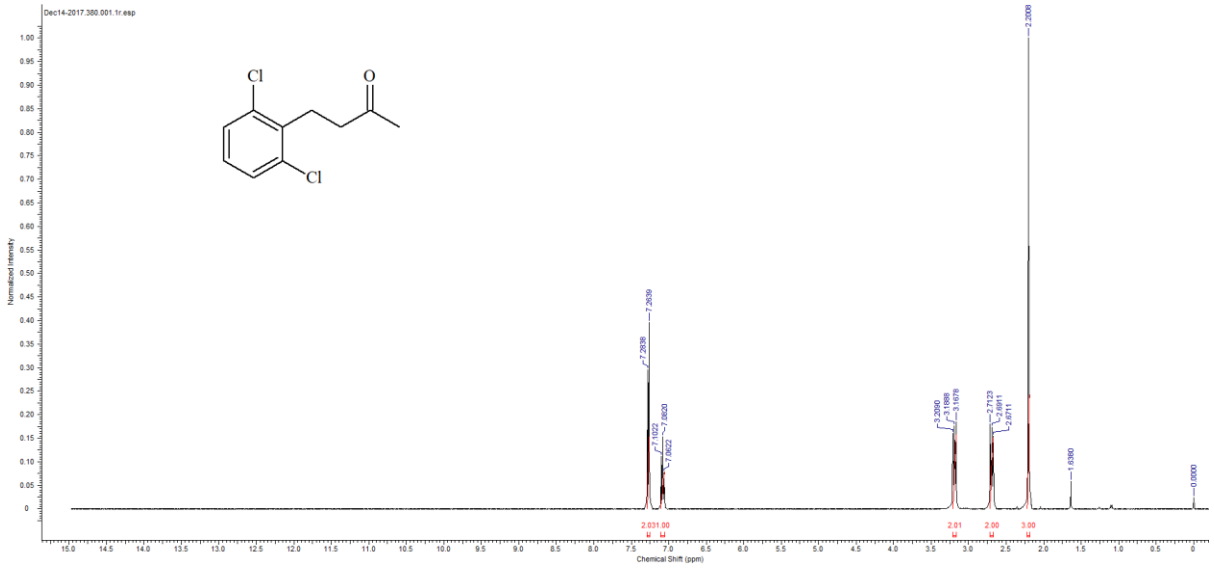

Dec14-2017.351.001.1r.esp
Cl
Cl
O
Normalized Intensity
Chemical Shift (ppm)
207.1605
137.1631
134.4703
131.4621
129.2765
127.1566
77.3469
77.0329
76.7112
42.9020
29.9728
27.1917


Dec14-2017.360.001.1r.esp
Cl
O
Normalized Intensity
Chemical Shift (ppm)
7.1899
7.1207
7.1119
7.1004
7.0960
7.0912
2.9154
2.7971
2.6793
2.6608
2.0734
1.5419
0.0001
3.07 1.00
2.02 2.03
3.02

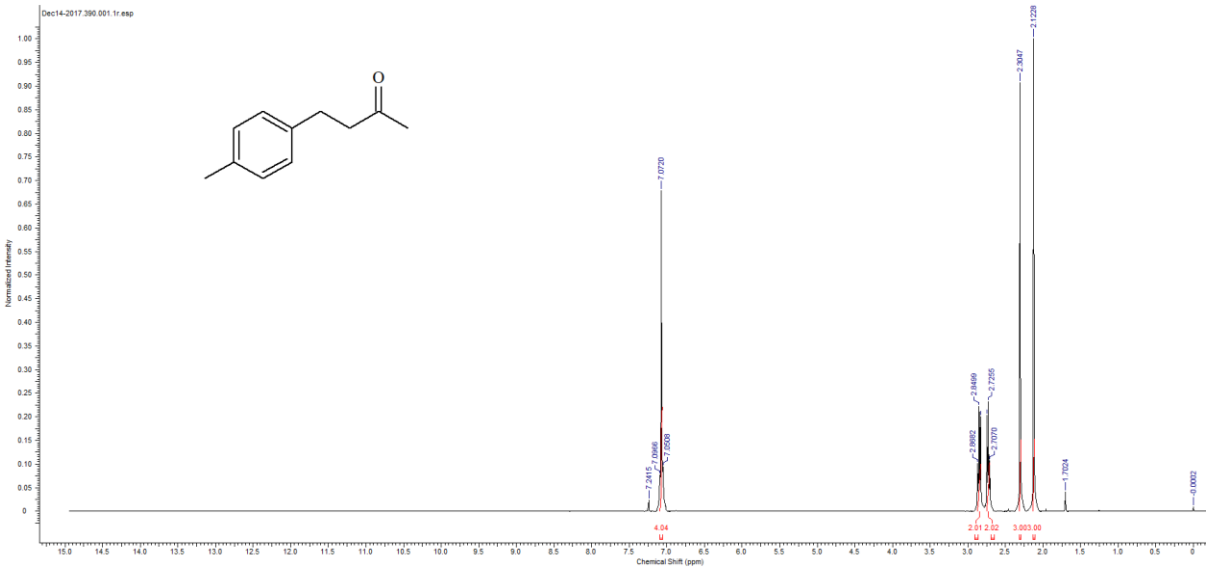

Dec14-2017.361.001.1r.esp
Cl
O
Normalized Intensity
Chemical Shift (ppm)
207.2884
143.0733
134.2412
129.7981
128.4513
126.5747
126.3219
77.3469
76.7112
44.7250
30.0947
29.2528

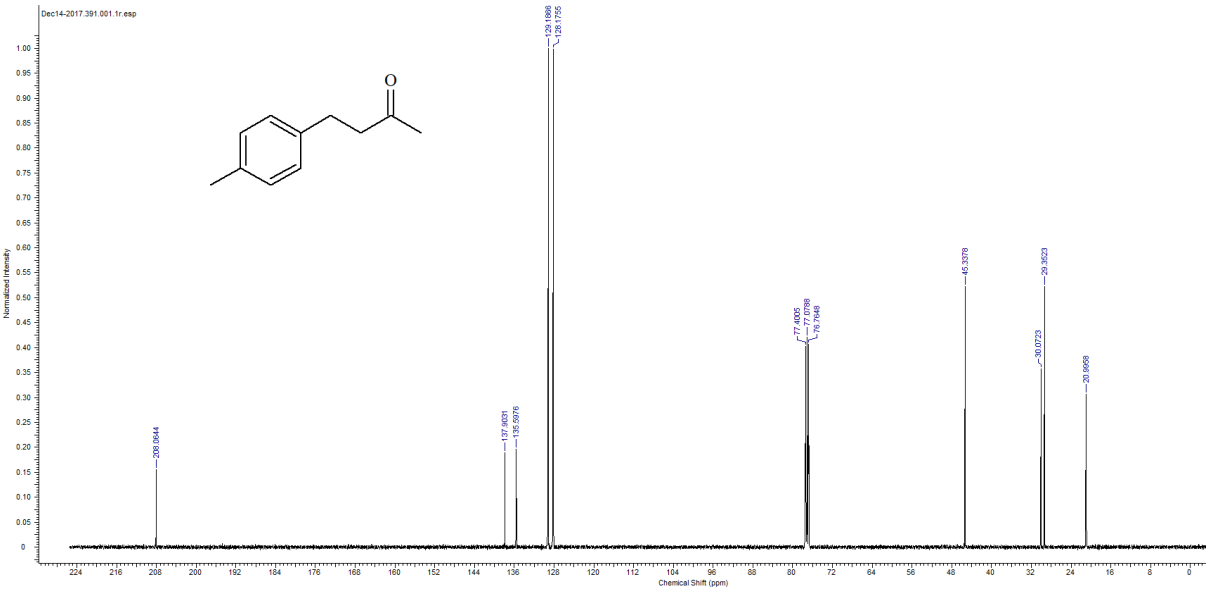

Dec14-2017.370.001.1r.esp
F
O
Cl
Normalized Intensity
Chemical Shift (ppm)

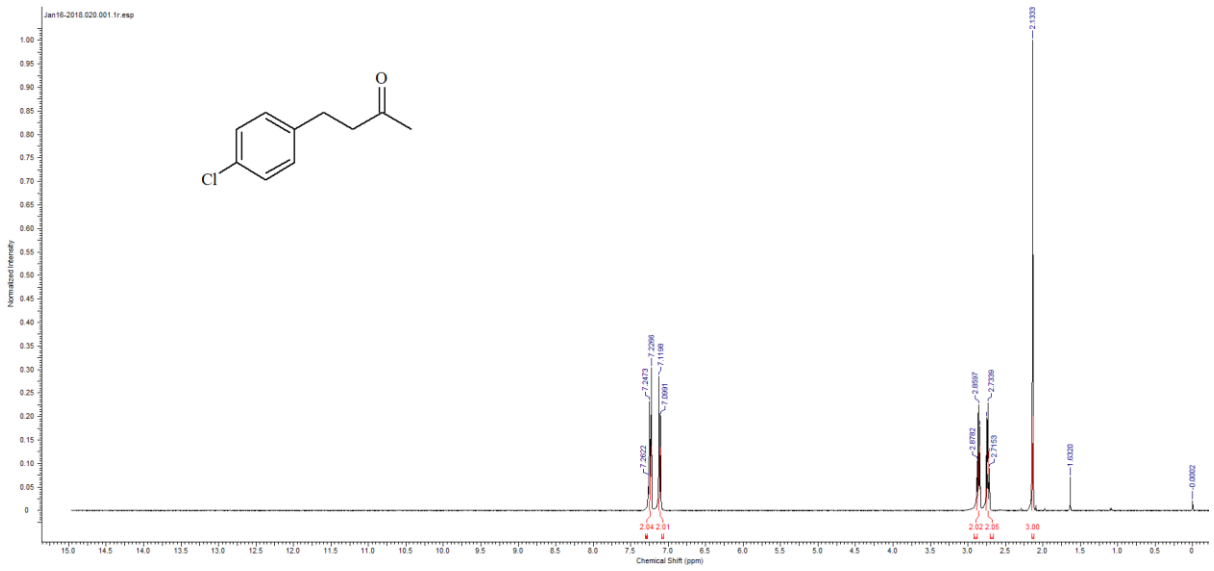

Dec14-2017.371.001.1r.esp
F
O
Cl
Normalized Intensity
Chemical Shift (ppm)


Dec14-2017.380.001.1r.esp
Cl
O
Cl
Normalized Intensity
Chemical Shift (ppm)


Dec14-2017.381.001.1r.esp
Cl
O
Cl
Normalized Intensity
Chemical Shift (ppm)
128.2062
77.3469
76.7112
127.9074
41.4236
25.5702
29.7353
207.2295
136.8001
135.2529

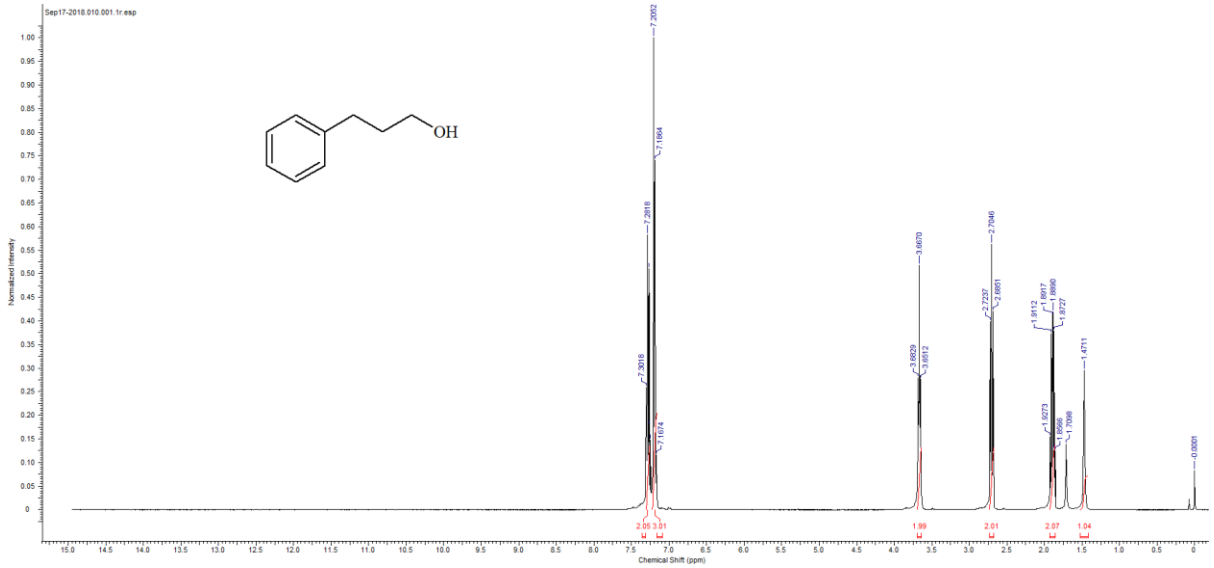

Dec14-2017.390.001.1r.esp
O
Normalized Intensity
Chemical Shift (ppm)
7.0720
2.1228
2.3047
2.8499
2.7255
2.8982
2.7070
7.3415
7.1998
7.3508
1.7024
0.0002
4.04
2.01
2.02
3.003.00

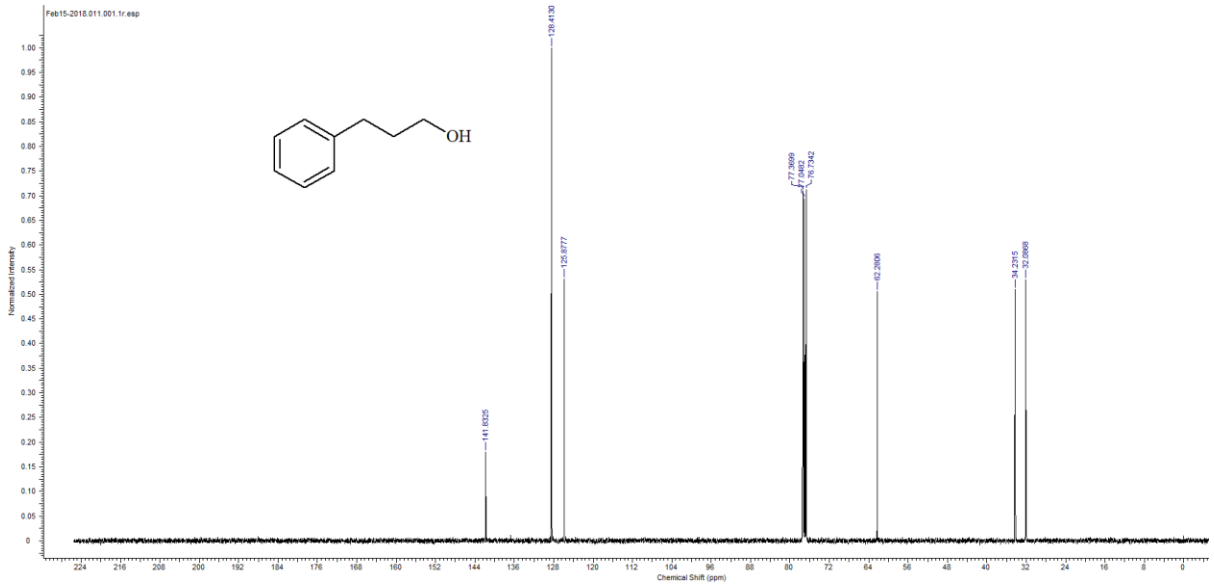

Dec14-2017.391.001.1r.esp
O
Normalized Intensity
Chemical Shift (ppm)
129.1999
128.1755
45.3378
29.3523
77.4005
77.0788
76.7568
30.0723
20.9658
209.0644
137.9031
135.5976

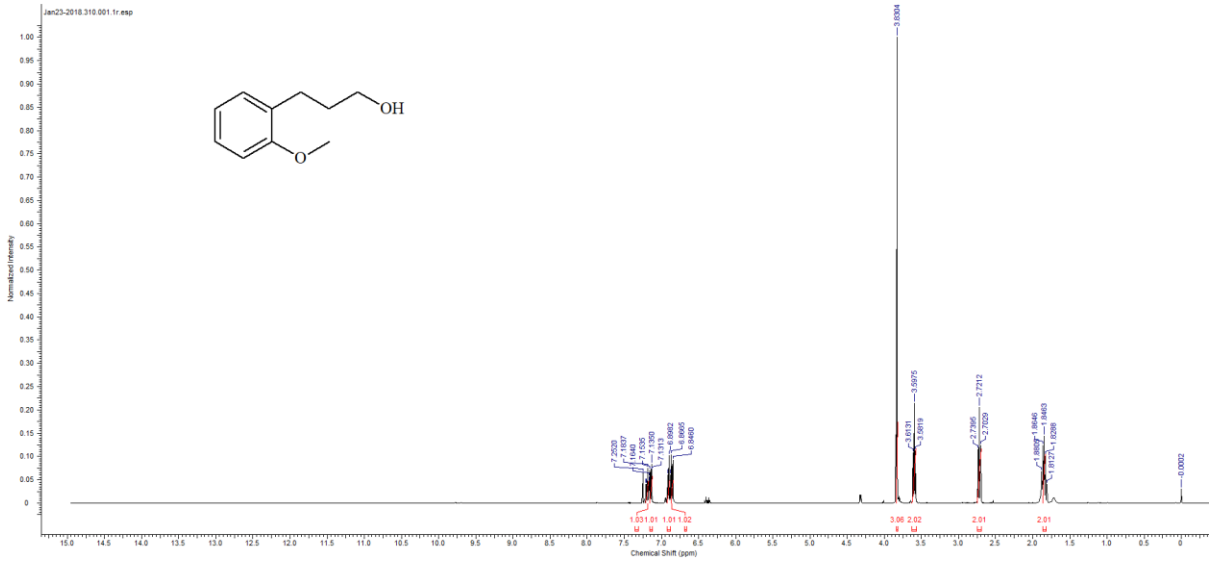

Jan16-2018.020.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
Cl
O
7.2473
7.2295
7.1196
7.0901
7.2822
2.9997
2.7339
2.8762
2.7153
2.1333
1.6328
0.0002
2.04
2.01
2.02
2.05
3.00

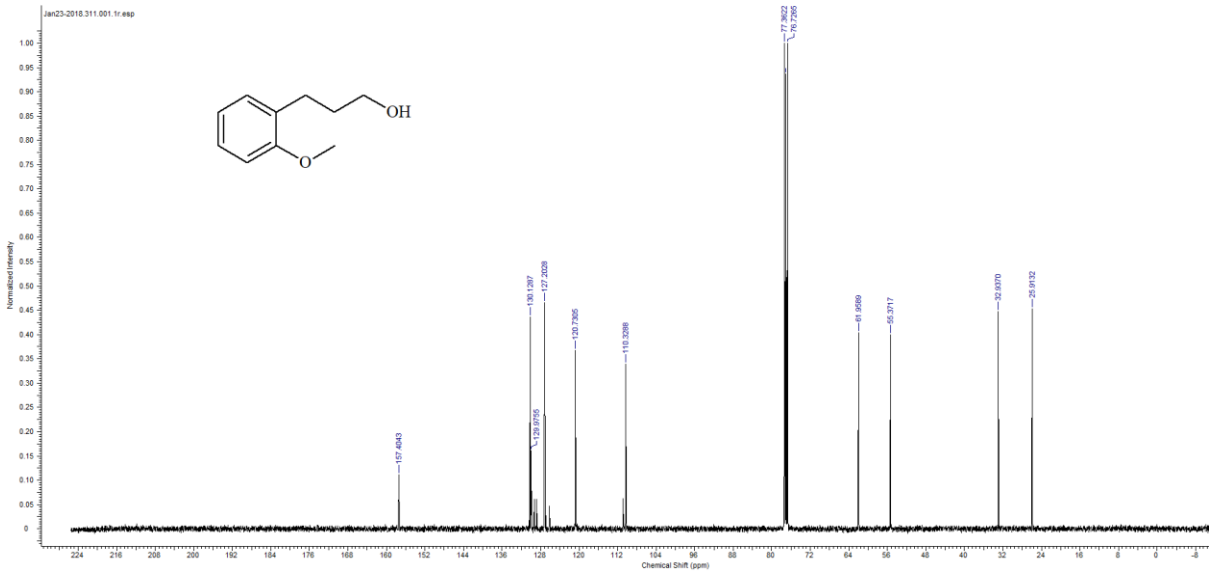

Jan16-2018.021.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
Cl
O
207.4593
139.4810
131.8598
129.6999
126.5736
77.3546
76.7188
44.8935
30.0877
26.9847

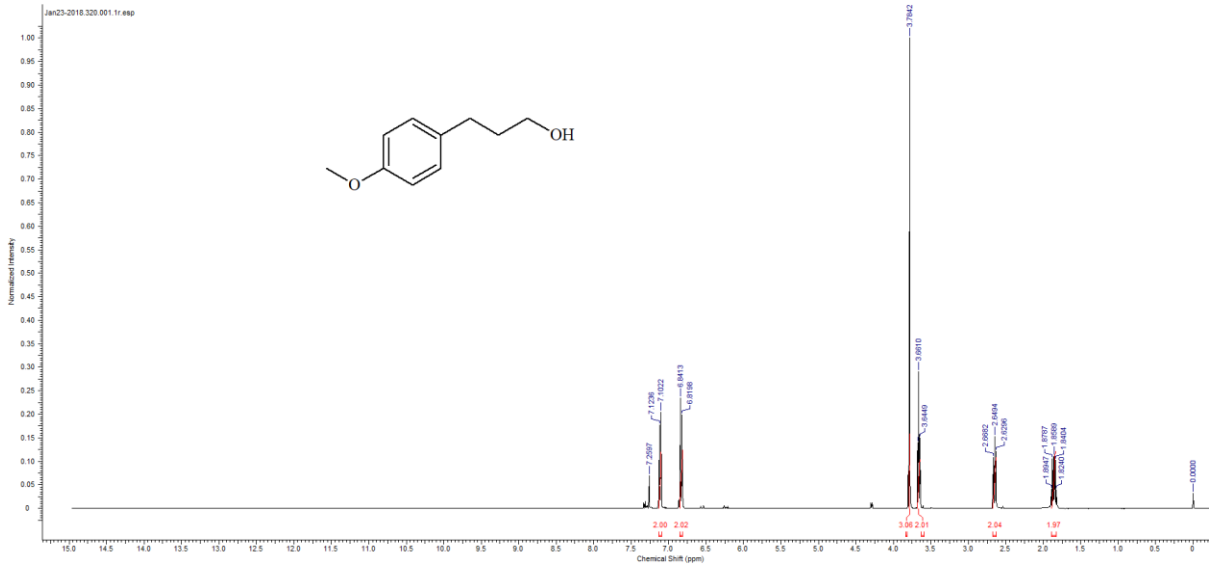
Copies of NMR spectra for the reduction of unsaturated aldehydes with methanol

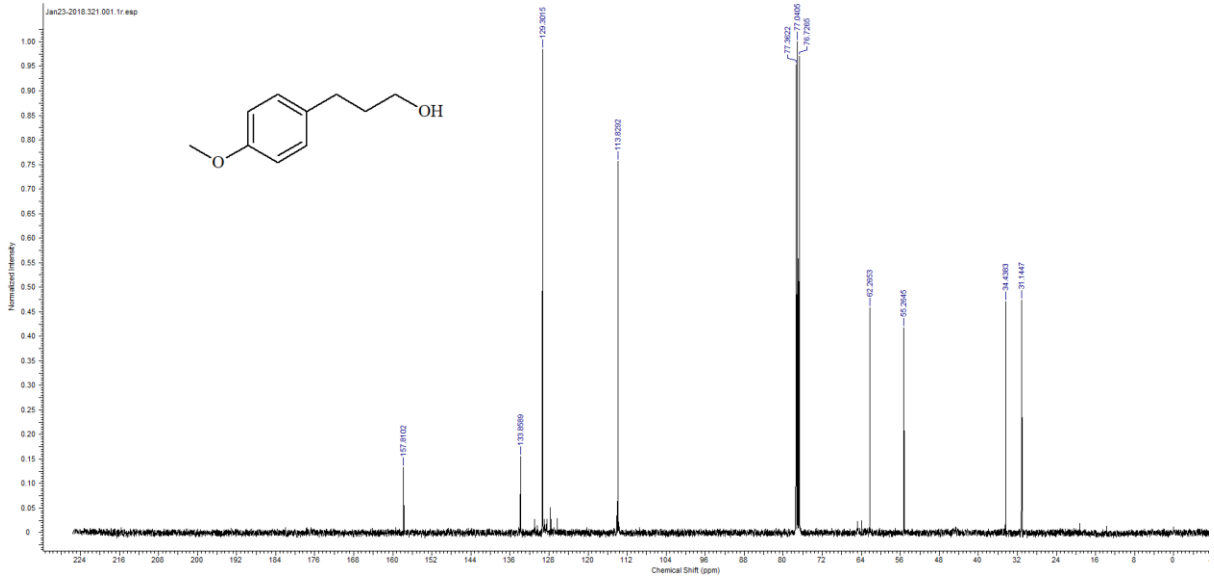


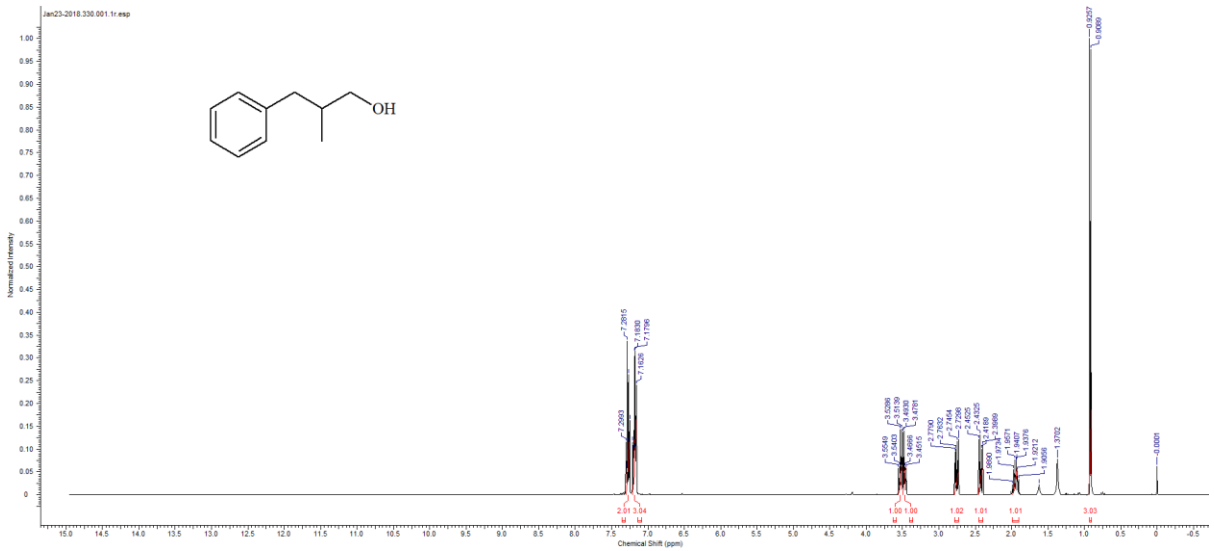


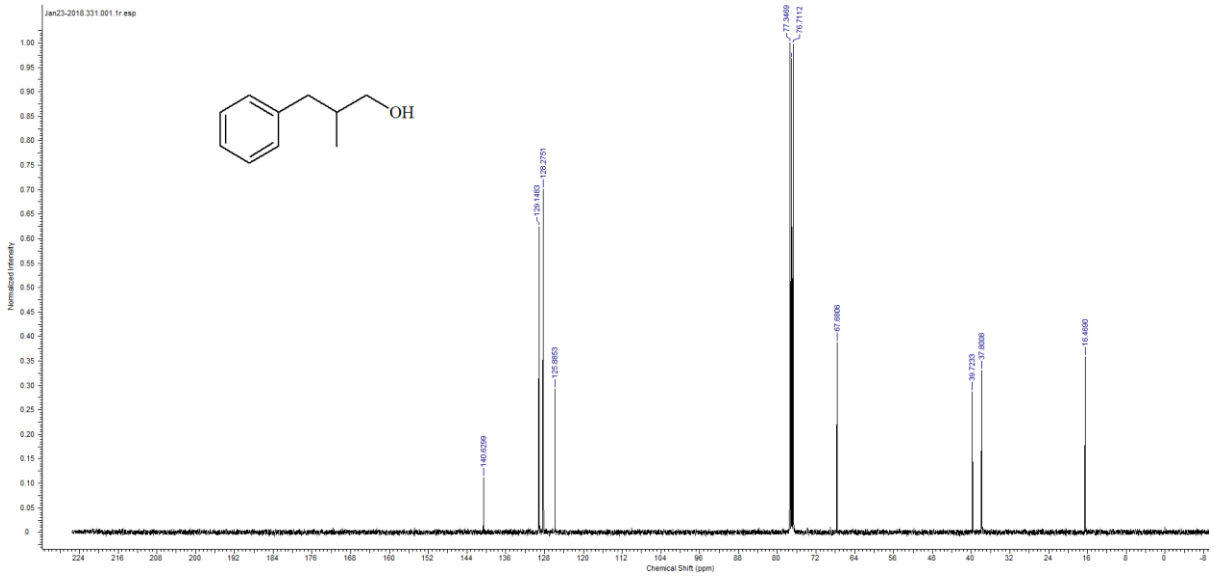


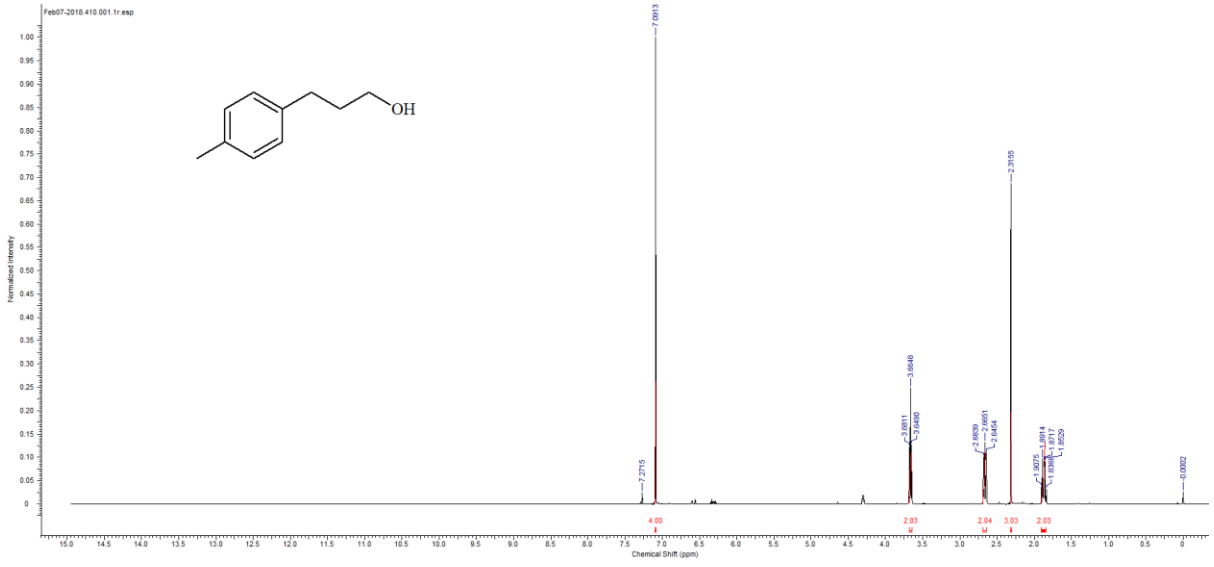

Jan23-2018.311.001.1r.esp
OH
O
Normalized Intensity
Chemical Shift (ppm)
77.3622
76.7265
130.1297
127.2039
120.7305
115.3288
81.9689
55.3717
32.6370
25.9132
157.4843
129.9755

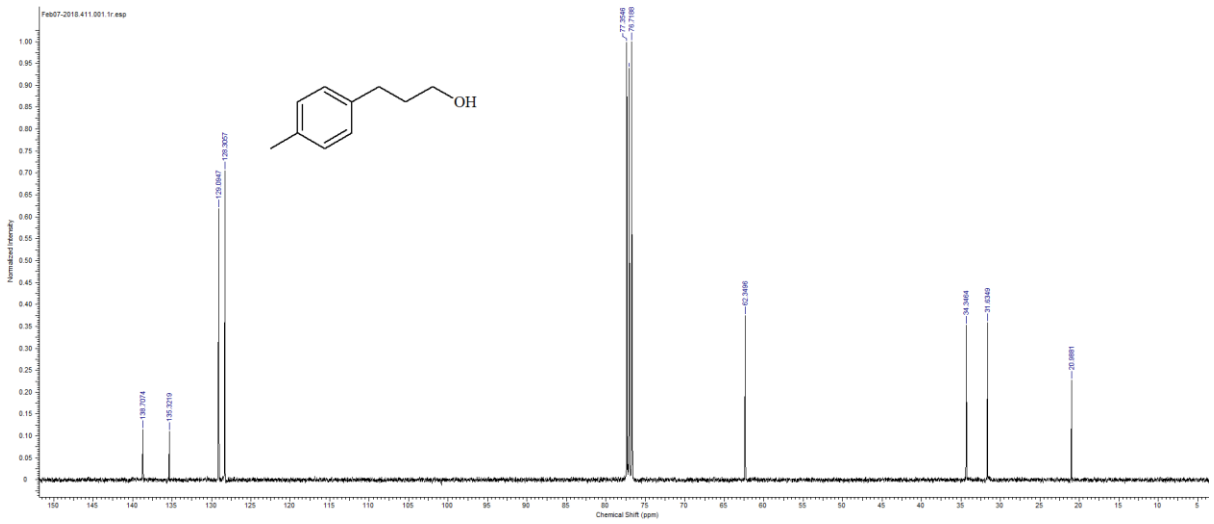

Jan23-2018.320.001.1r.esp
OH
O
Normalized Intensity
Chemical Shift (ppm)
3.7942
3.6910
3.6449
7.2597
7.1296
7.1022
6.8413
6.8198
2.6992
2.6494
2.6296
1.8697
1.8599
1.8404
1.8240
0.0000
2.00
2.02
3.06
2.01
2.04
1.97

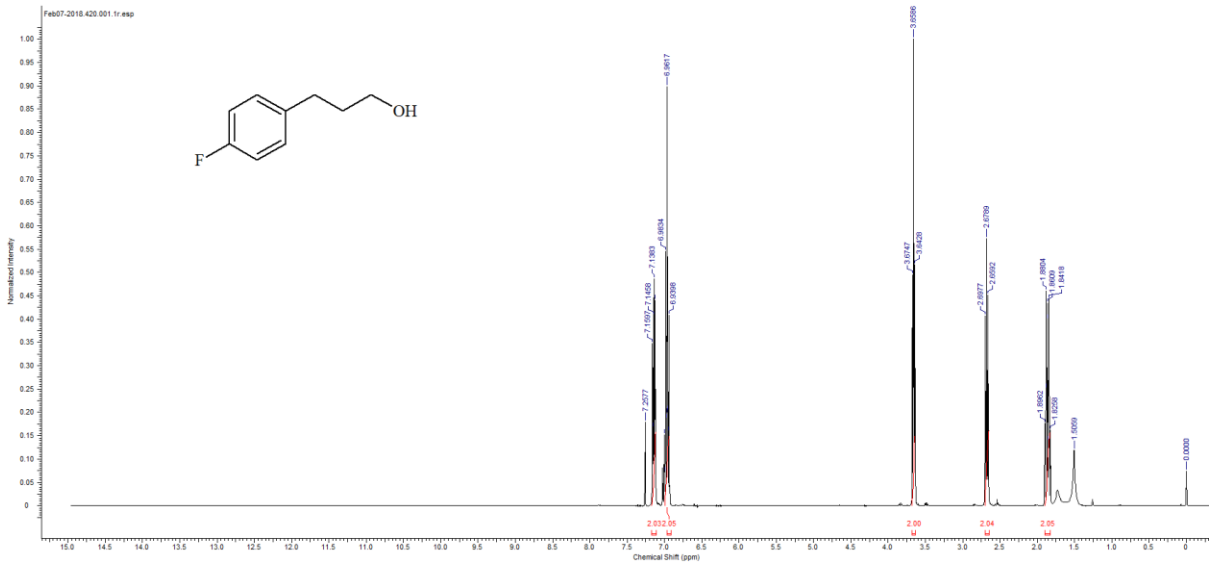

Jan23-2018.321.001.1r.esp
OH
O
Normalized Intensity
Chemical Shift (ppm)
129.3015
113.8292
77.3622
77.0405
76.7265
62.2653
55.3645
34.4383
31.1447
157.8102
133.8699

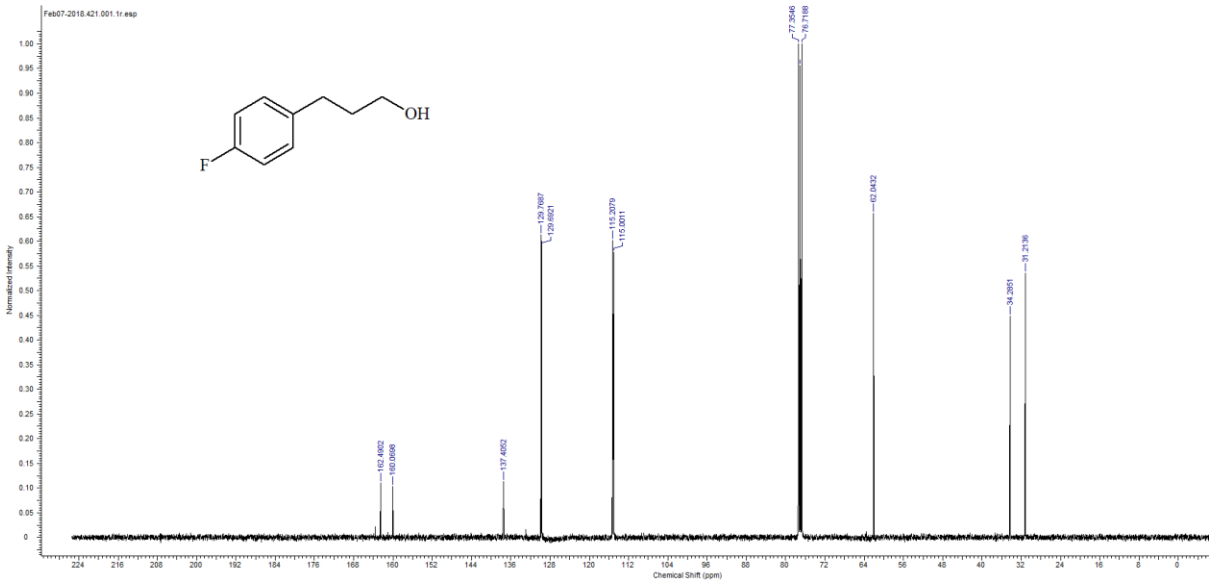

Jan23-2018.330.001.1r.esp
OH
Normalized Intensity
Chemical Shift (ppm)

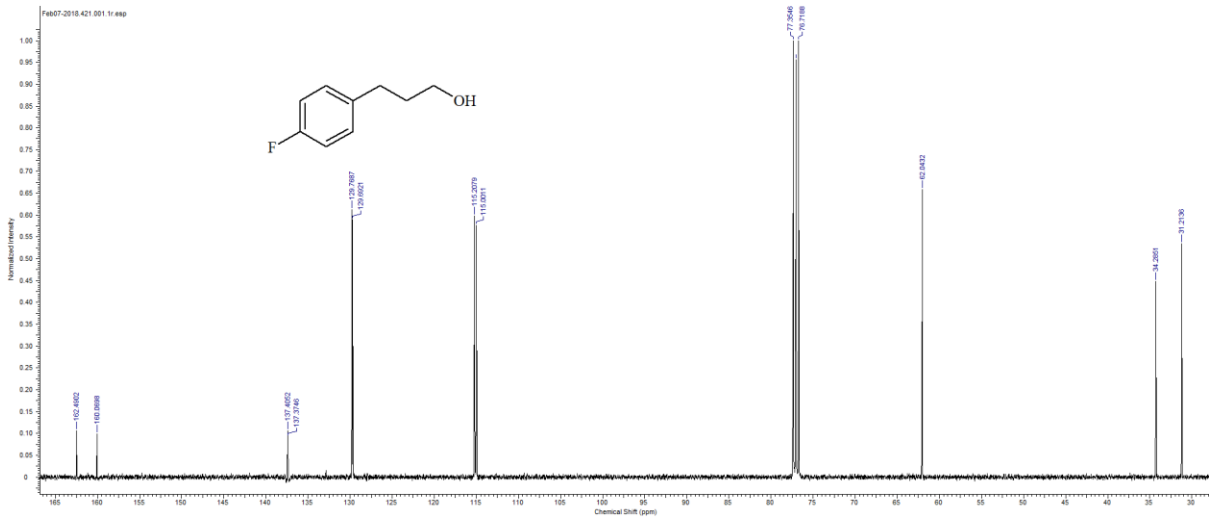

Jan23-2018.331.001.1r.esp
OH
Normalized Intensity
Chemical Shift (ppm)

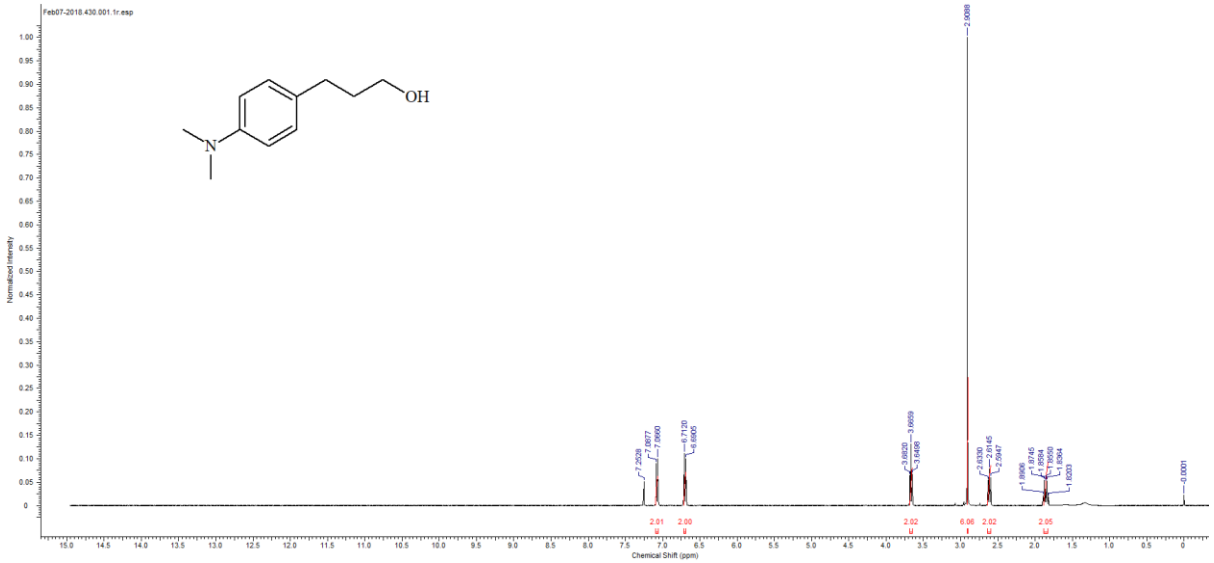

Feb07-2018.410.001.1r.esp
OH
Normalized Intensity
Chemical Shift (ppm)

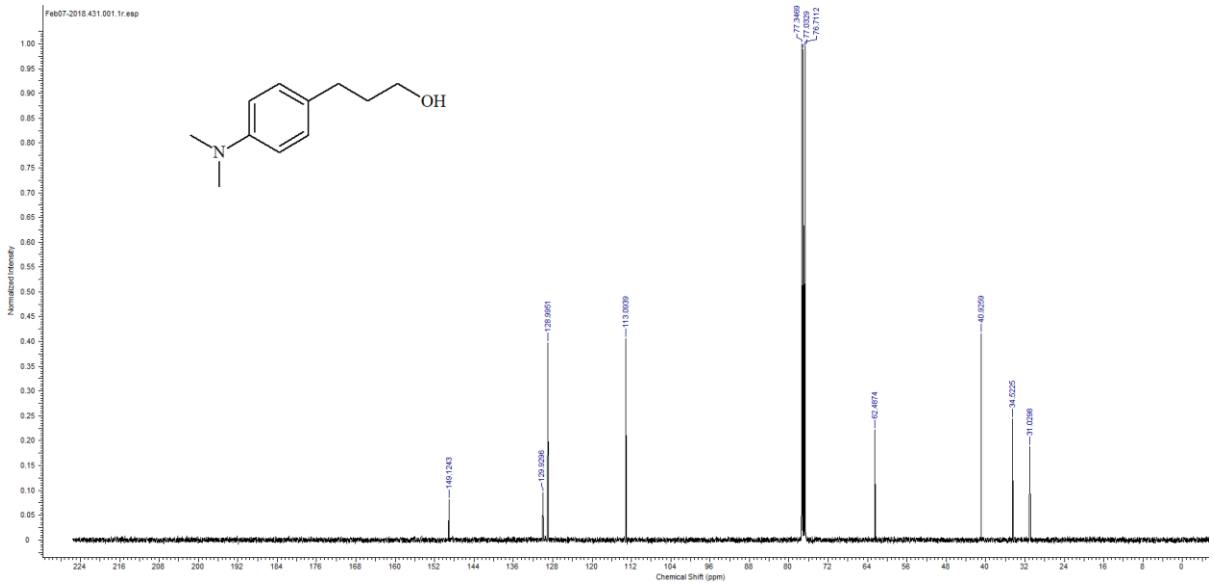

Feb07-2018.411.001.1r.esp
OH
Normalized Intensity
Chemical Shift (ppm)

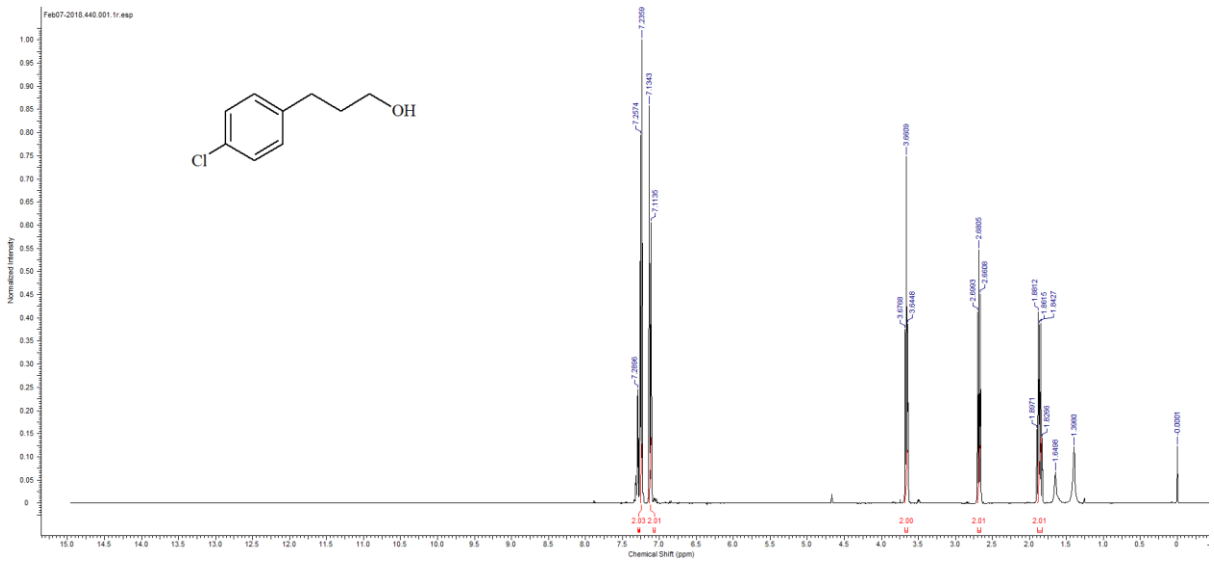

Feb07-2018.420.001.1r.esp
OH
F
Normalized Intensity
Chemical Shift (ppm)

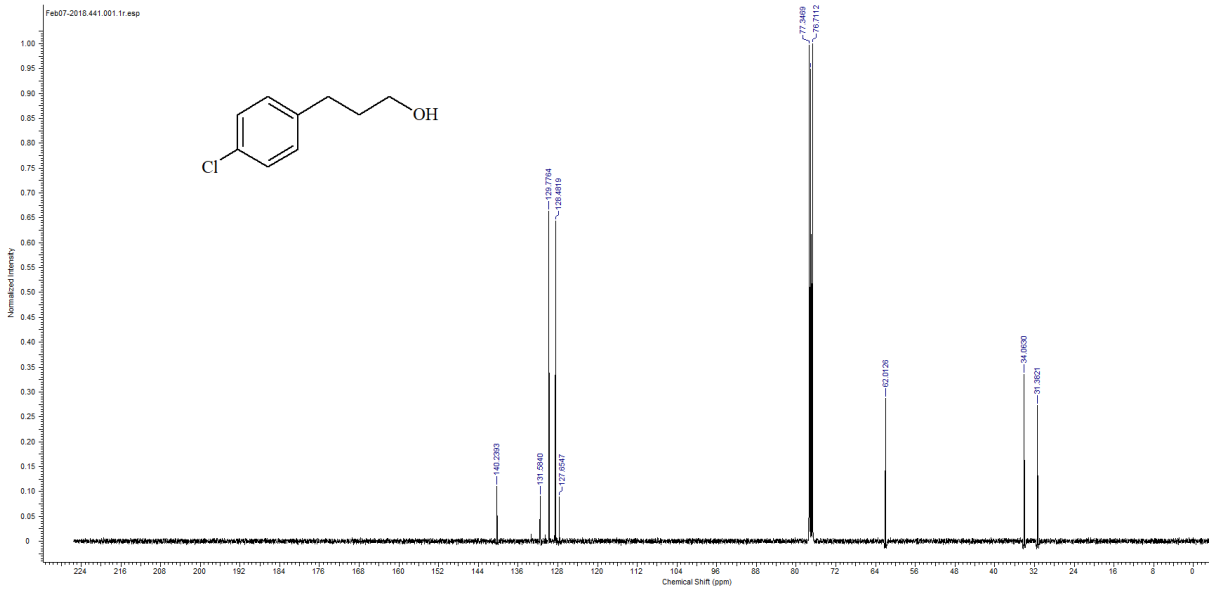

Feb07-2018.421.001.1r.esp
OH
F
Normalized Intensity
Chemical Shift (ppm)

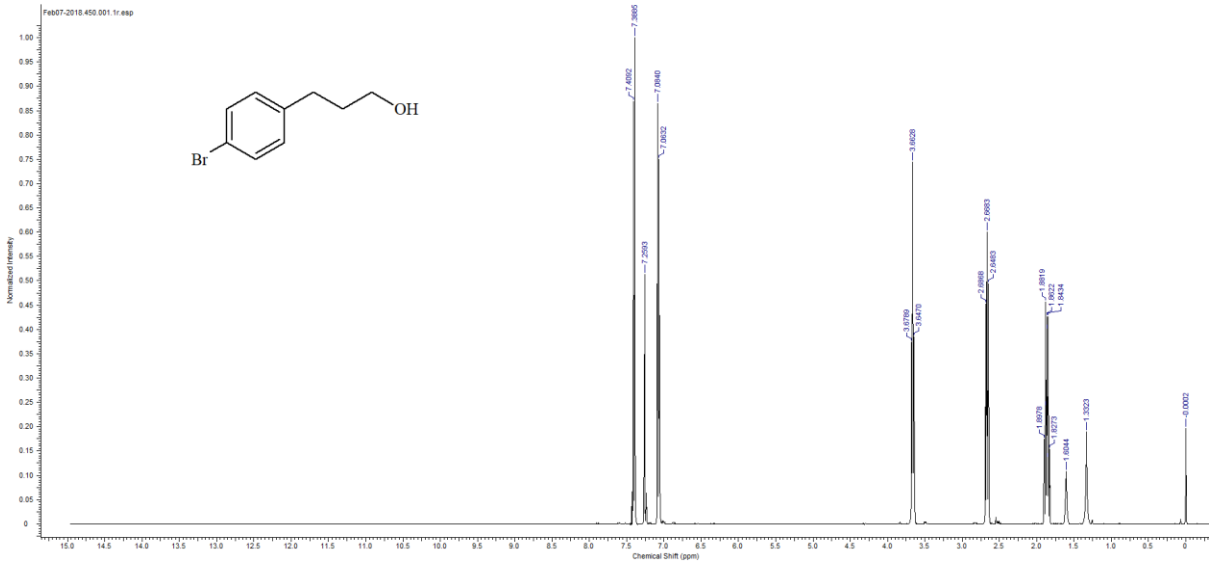

Feb07-2018.421.001.1r.esp
OH
F
Normalized Intensity
Chemical Shift (ppm)

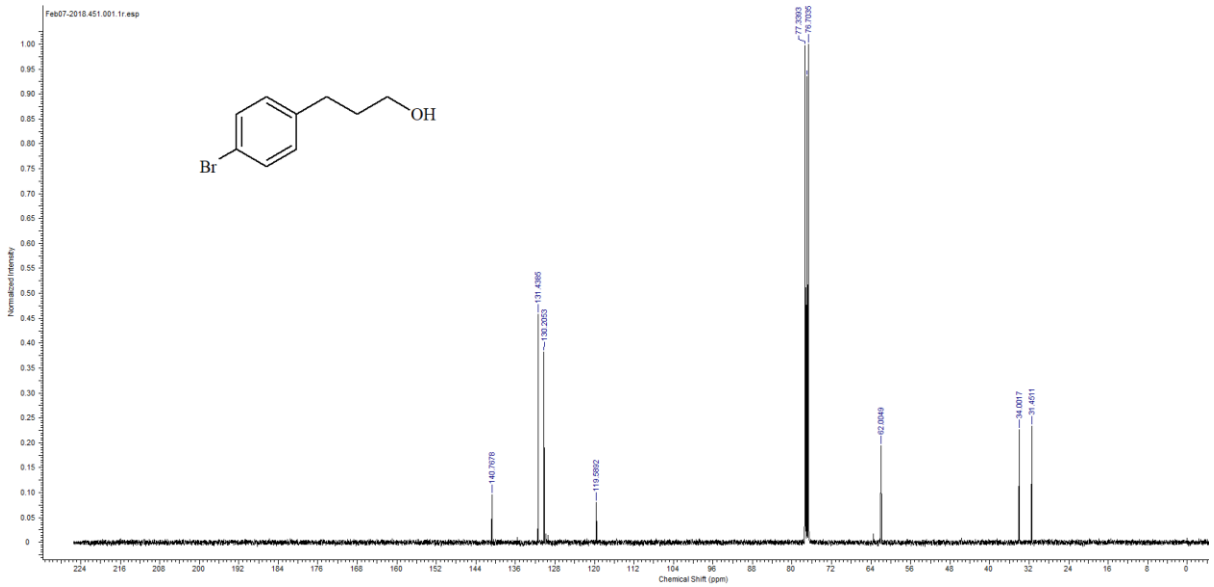

Feb07-2018.430.001.1r.esp
OH
N
Normalized Intensity
Chemical Shift (ppm)

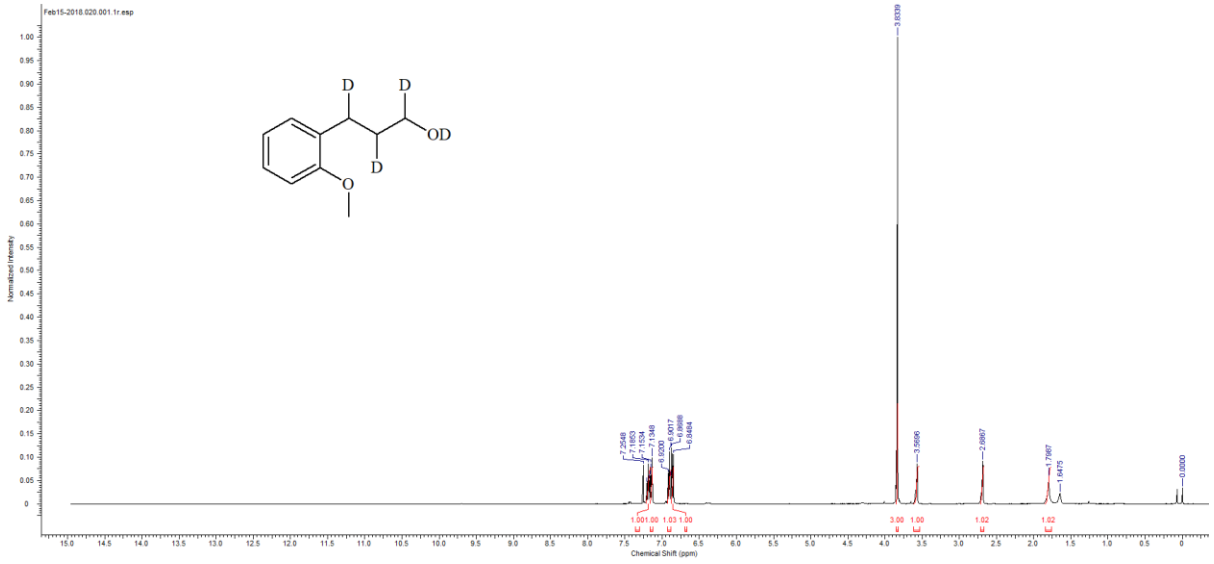

Feb07-2018.431.001.1r.esp
OH
N
Normalized Intensity
Chemical Shift (ppm)

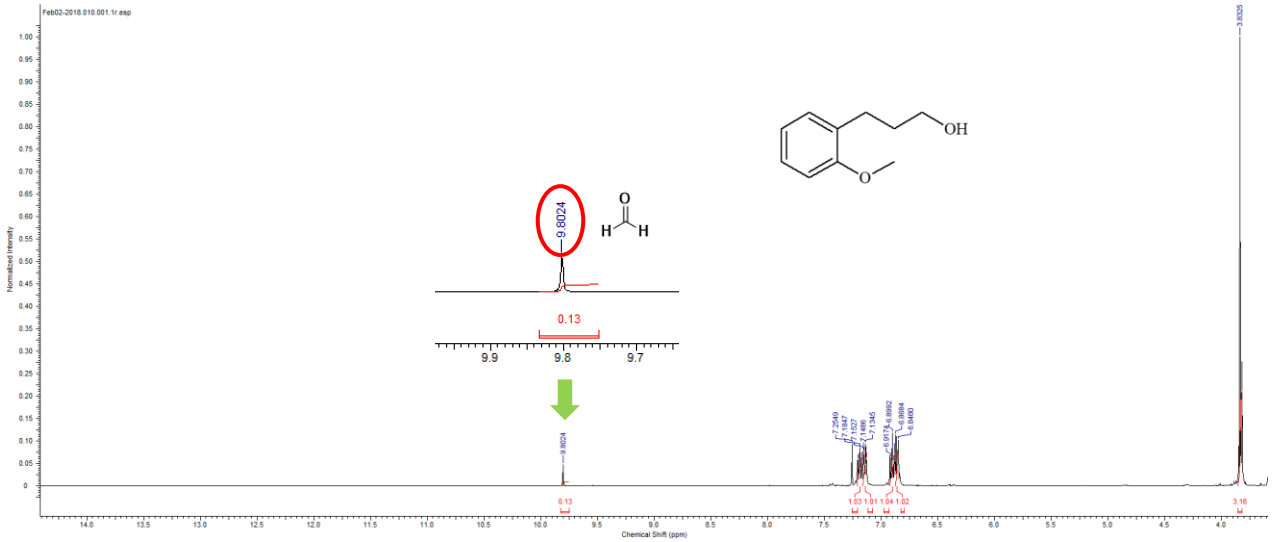

Feb07-2018.440.001.1r.esp
OH
Cl
Normalized Intensity
Chemical Shift (ppm)

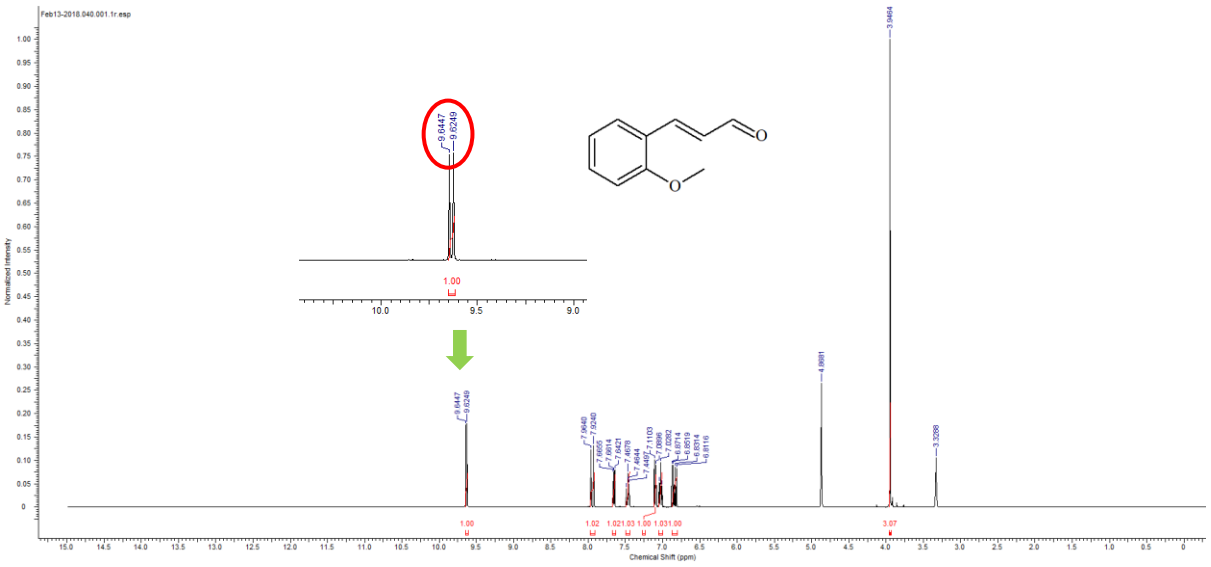

Feb07-2018.441.001.1r.esp
OH
Cl
Normalized Intensity
Chemical Shift (ppm)


Feb07-2018.450.001.1r.esp
OH
Br
Normalized Intensity
Chemical Shift (ppm)

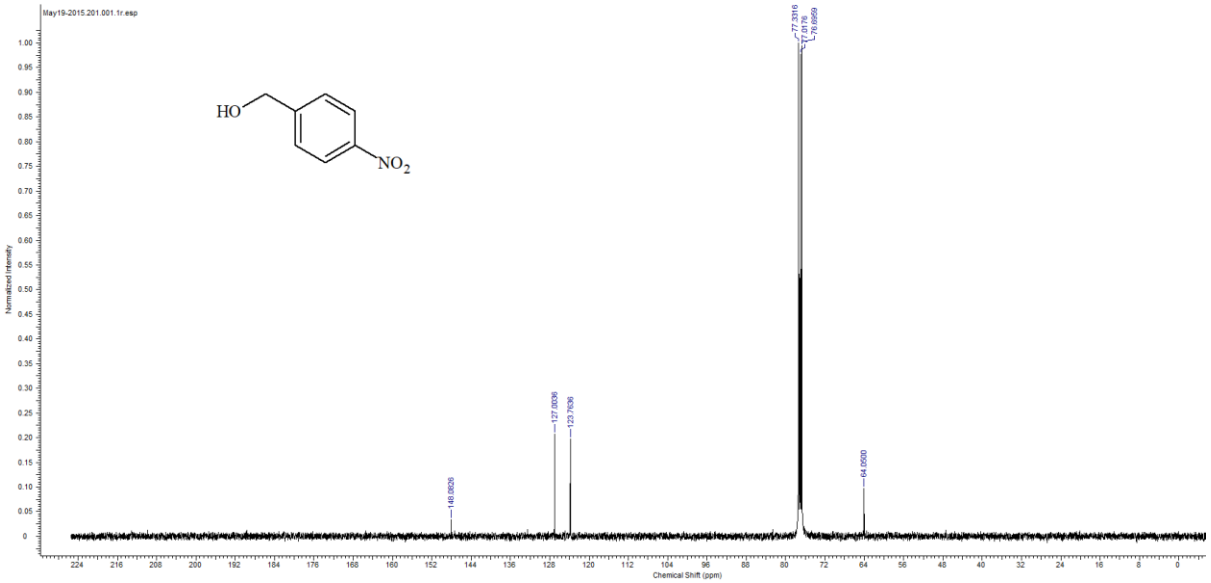

Feb07-2018.451.001.1r.esp
Br
OH
Normalized Intensity
Chemical Shift (ppm)
77.3393
76.7035
131.4365
130.2053
140.7676
119.5892
62.0049
34.0017
31.4511

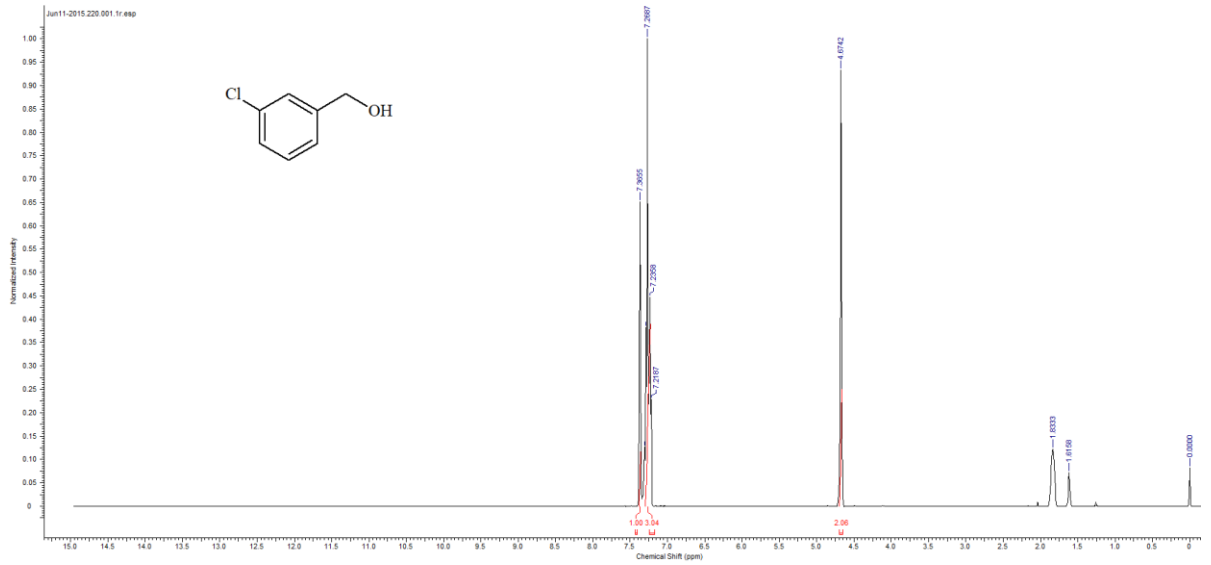

Feb15-2018.020.001.1r.esp
D
D
OD
D
O
Normalized Intensity
Chemical Shift (ppm)
3.6039
3.5996
2.8967
1.7967
1.6475
0.0000

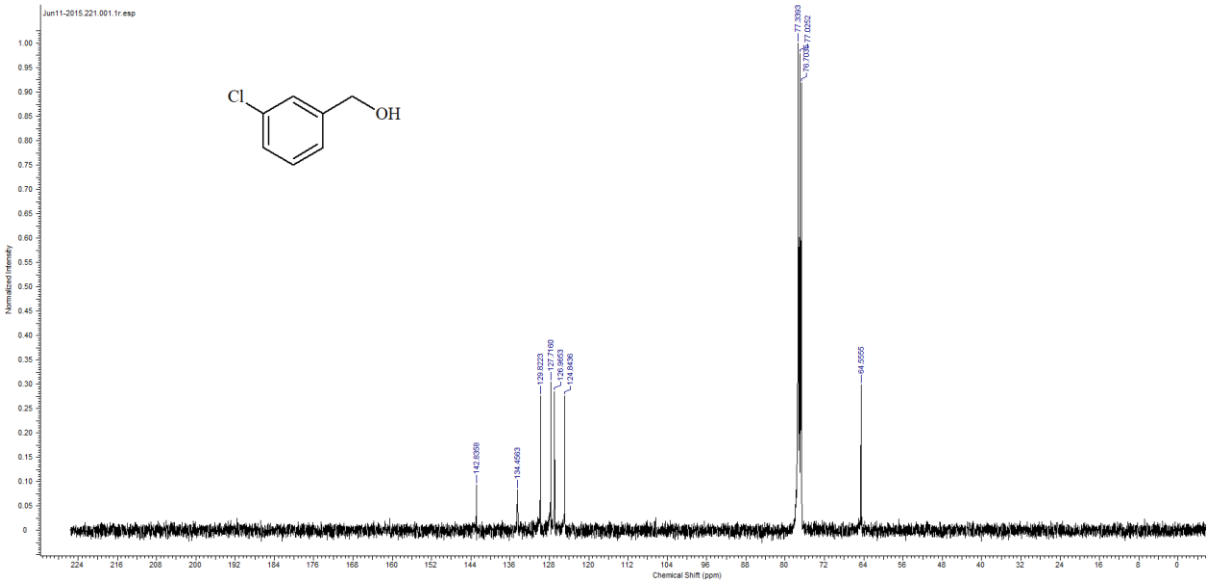

Feb02-2018.010.001.1r.esp
OH
O
9.8024
O
H
H
0.13
9.9
9.8
9.7
Normalized Intensity
Chemical Shift (ppm)
3.8325

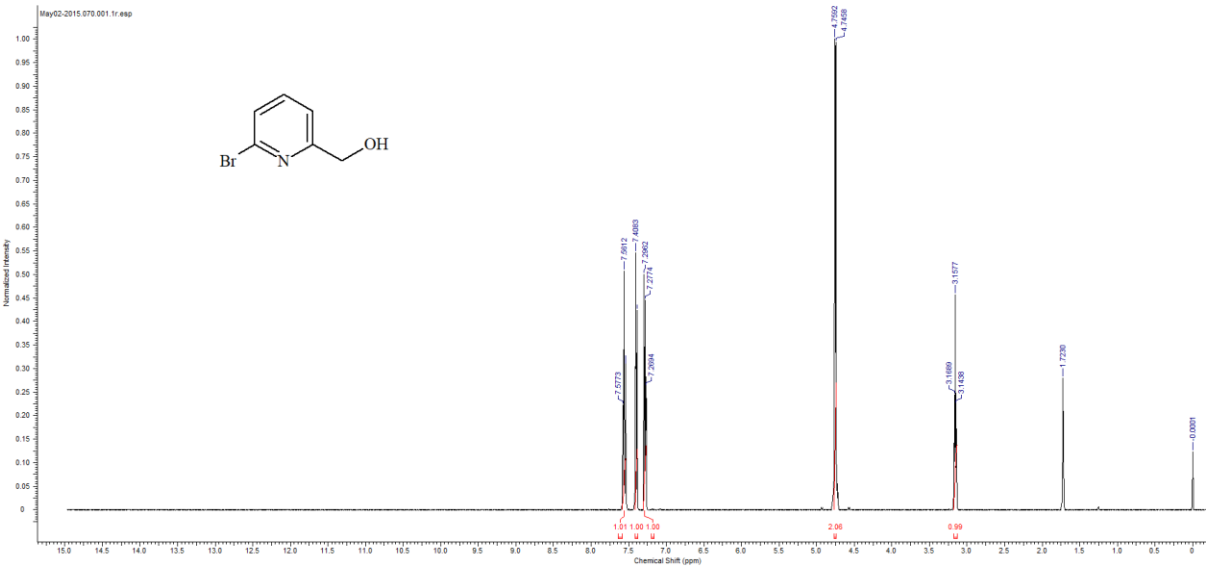


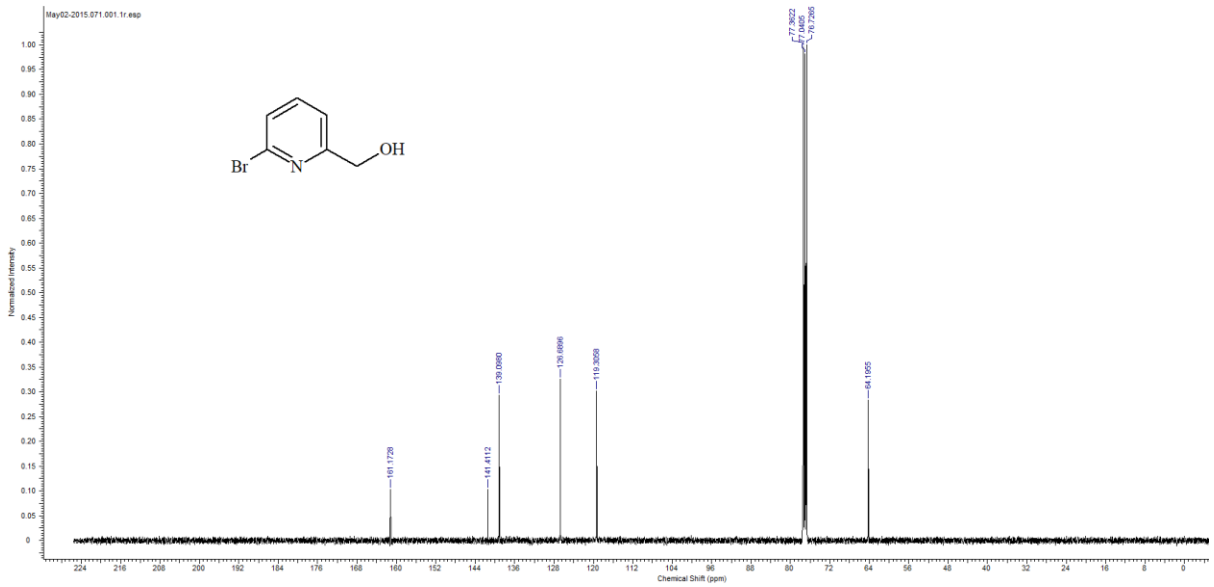
Copies of NMR spectra for the reduction of mono- and di-aldehydes

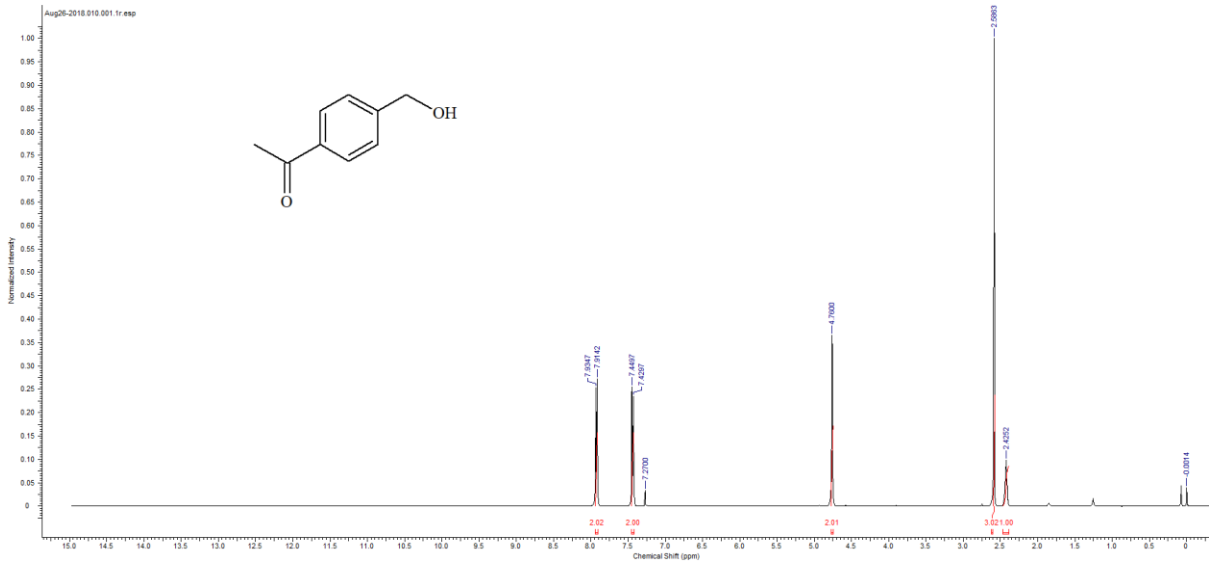


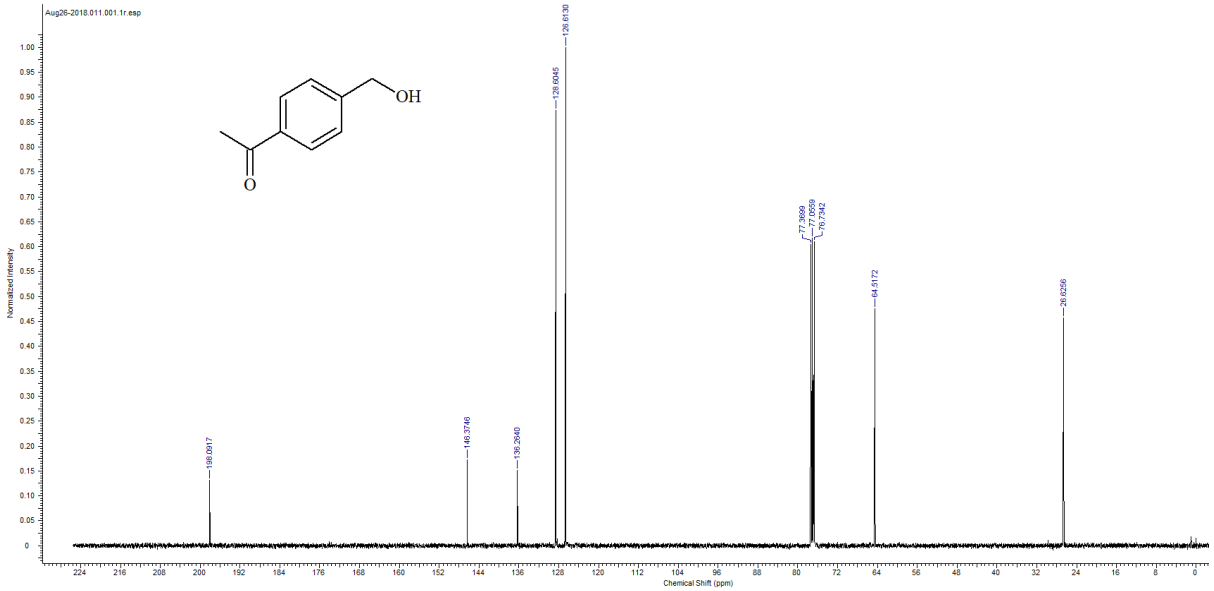

Jun11-2015.220.001.1r.esp
Cl
OH
7.2667
4.6742
7.3655
7.2359
7.2187
1.6333
1.6198
0.0000
1.00 3.04
2.06
Normalized Intensity
Chemical Shift (ppm)

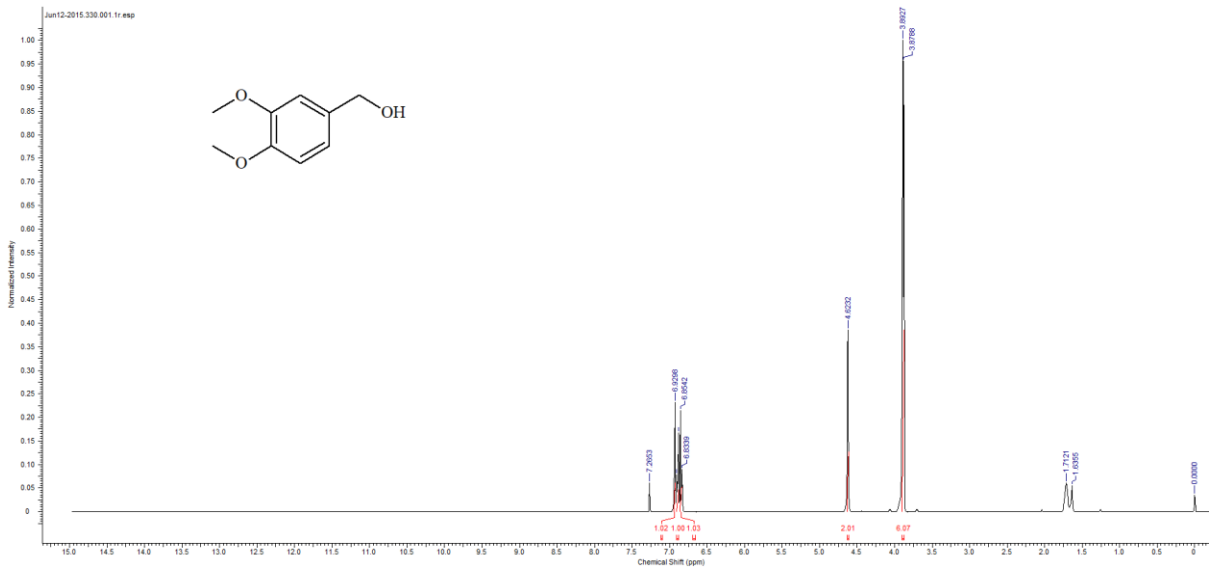

Jun11-2015.221.001.1r.esp
Cl
OH
77.3393
77.0252
142.8398
134.4553
129.6223
127.7160
126.9653
124.8436
64.5555
Normalized Intensity
Chemical Shift (ppm)

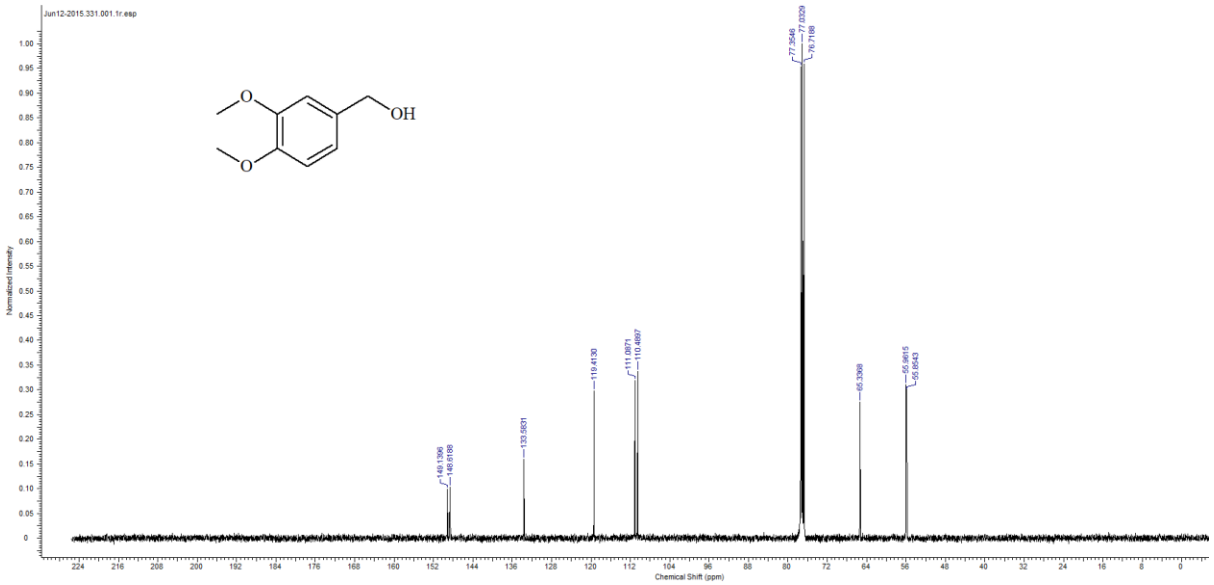

May02-2015.070.001.1r.esp
Br
N
OH
4.7692
4.7568
7.5912
7.4063
7.2862
7.2774
7.2694
7.5773
3.1577
3.1689
3.1438
1.7230
0.0001
1.01 1.00 1.00
2.06
0.99
Normalized Intensity
Chemical Shift (ppm)

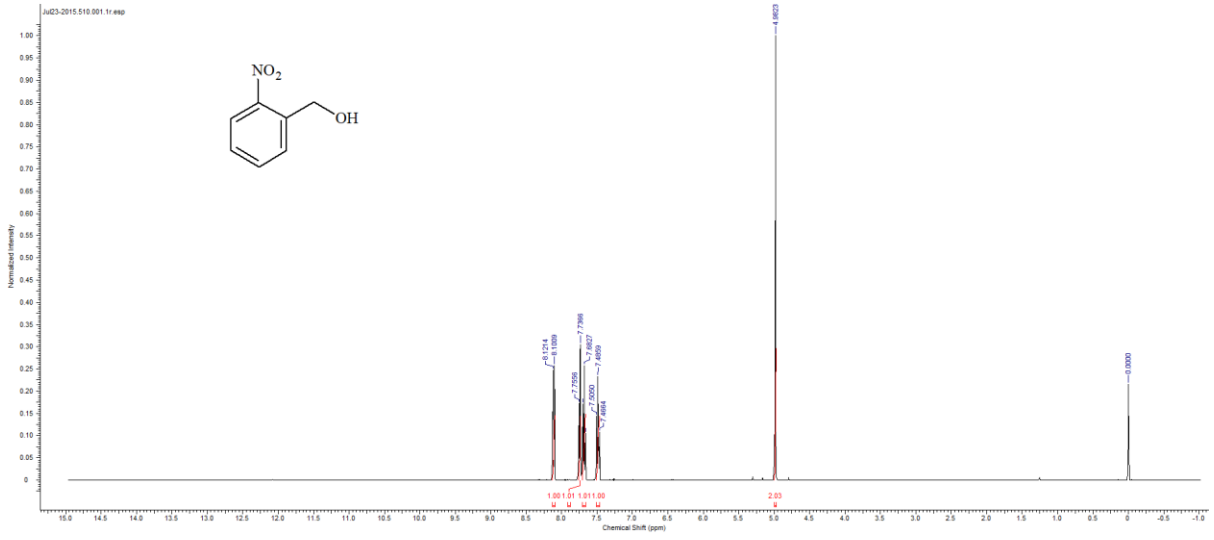

May02-2015.071.001.1r.esp
Br
N
OH
Normalized Intensity
Chemical Shift (ppm)
77.3622
77.0465
76.7295
161.1729
141.4112
139.0860
126.6896
119.3659
64.1955

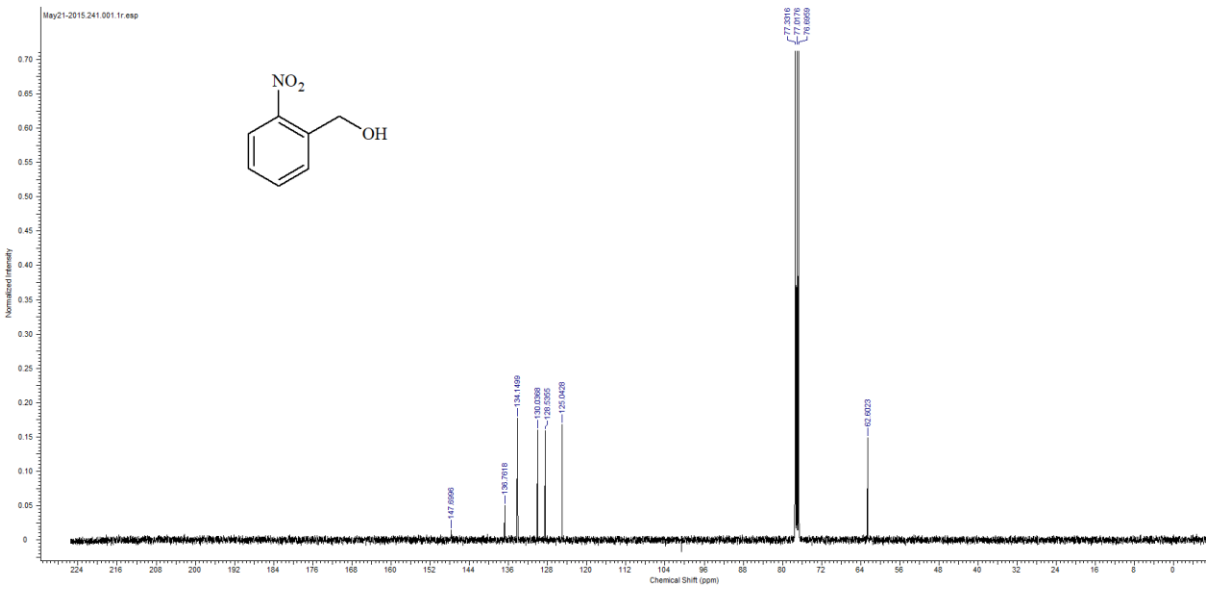

Aug26-2018.010.001.1r.esp
OH
O
Normalized Intensity
Chemical Shift (ppm)
7.9344
7.9142
7.4497
7.4297
7.2700
4.7009
2.5983
2.4252
0.0014
2.02
2.00
2.01
3.02
1.00

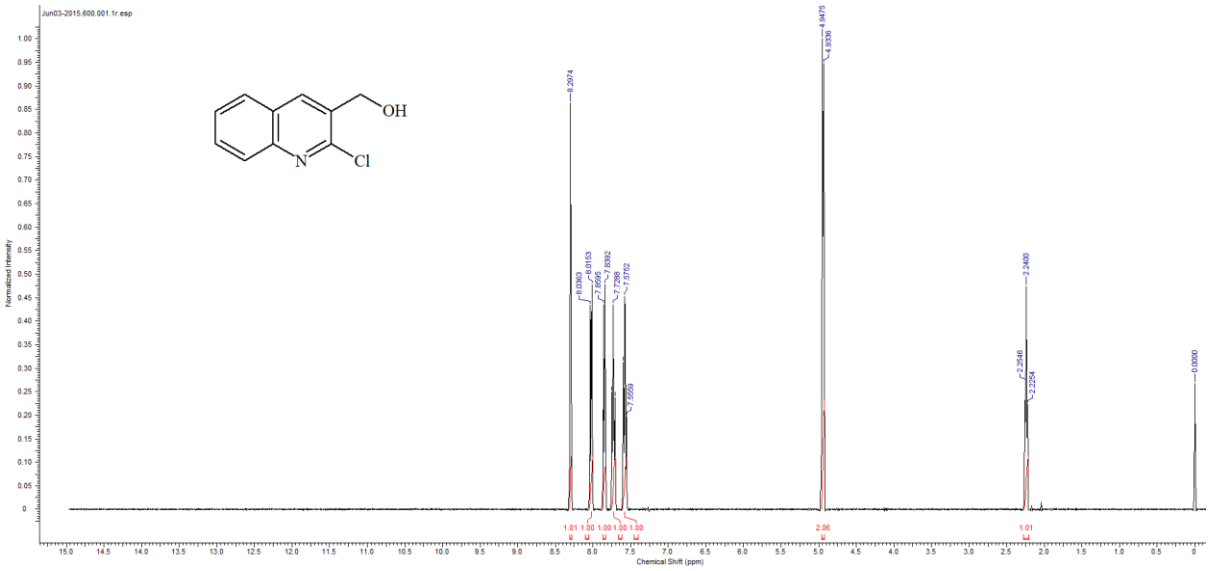

Aug26-2018.011.001.1r.esp
OH
O
Normalized Intensity
Chemical Shift (ppm)
126.6130
126.6045
77.3699
77.0559
76.7342
64.5172
26.6256
198.0317
146.3746
136.2640

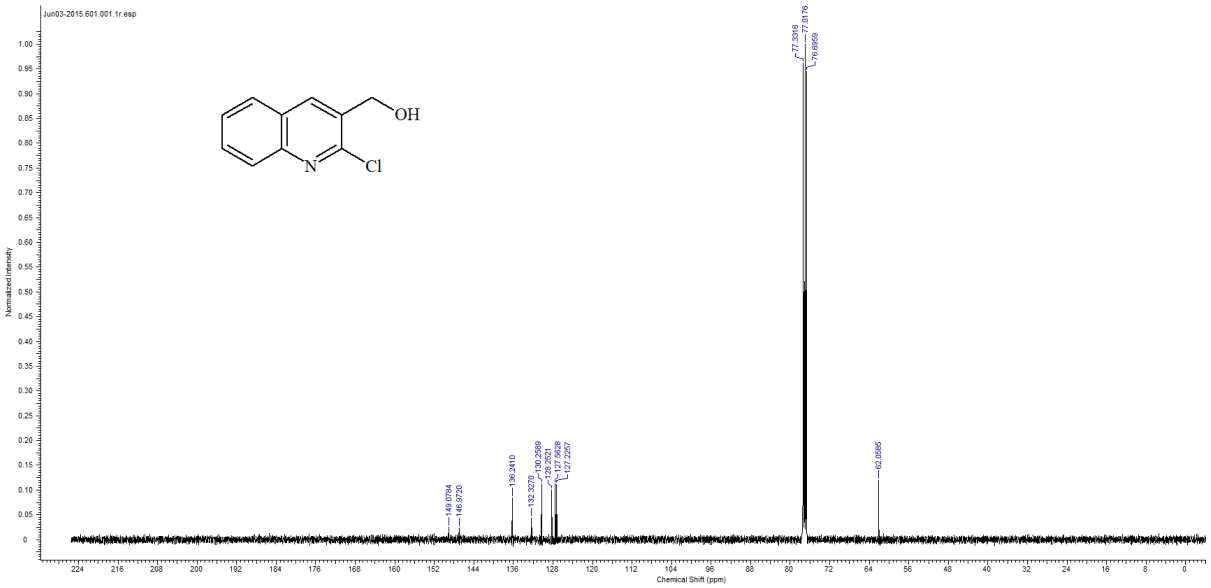

Jun12-2015.330.001.1r.esp
O
O
OH
Normalized Intensity
Chemical Shift (ppm)

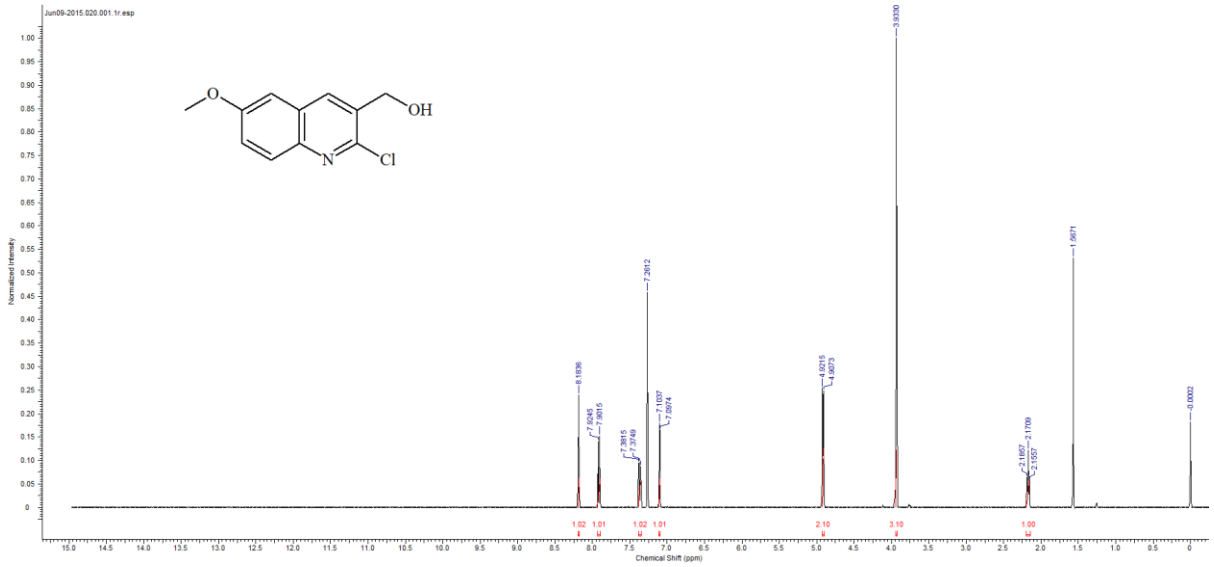

Jun12-2015.331.001.1r.esp
O
O
OH
Normalized Intensity
Chemical Shift (ppm)

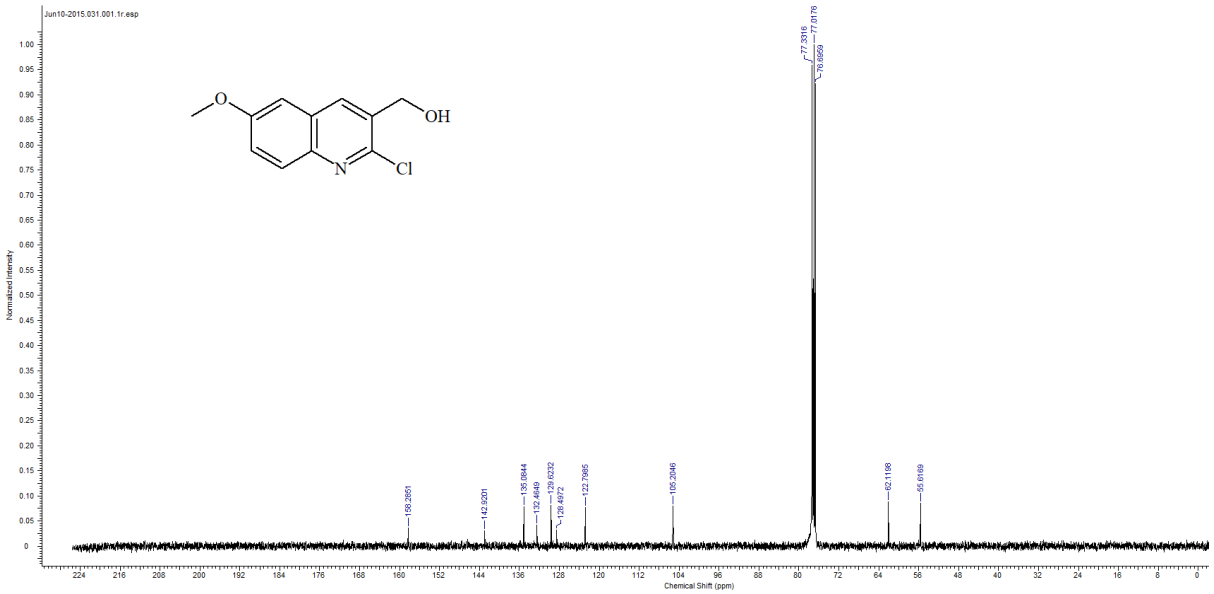

Jul23-2015.510.001.1r.esp
NO2
OH
Normalized Intensity
Chemical Shift (ppm)

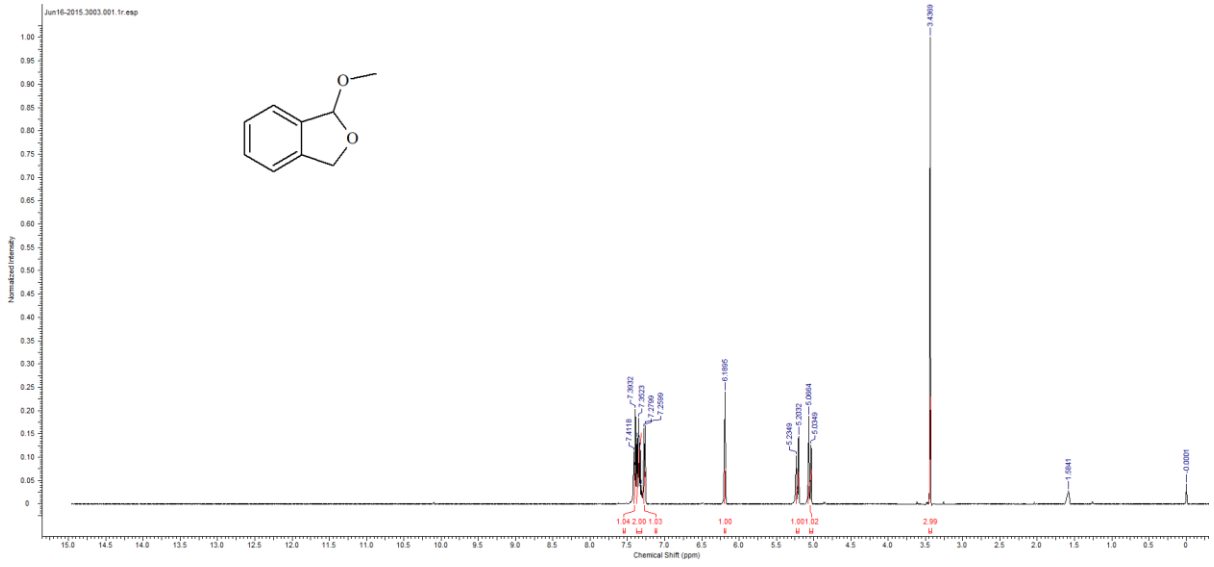

May21-2015.241.001.1r.esp
NO2
OH
77.3316
77.0176
76.6959
147.6996
136.7618
134.1499
130.0398
126.0355
125.0428
62.6023
Normalized Intensity
Chemical Shift (ppm)

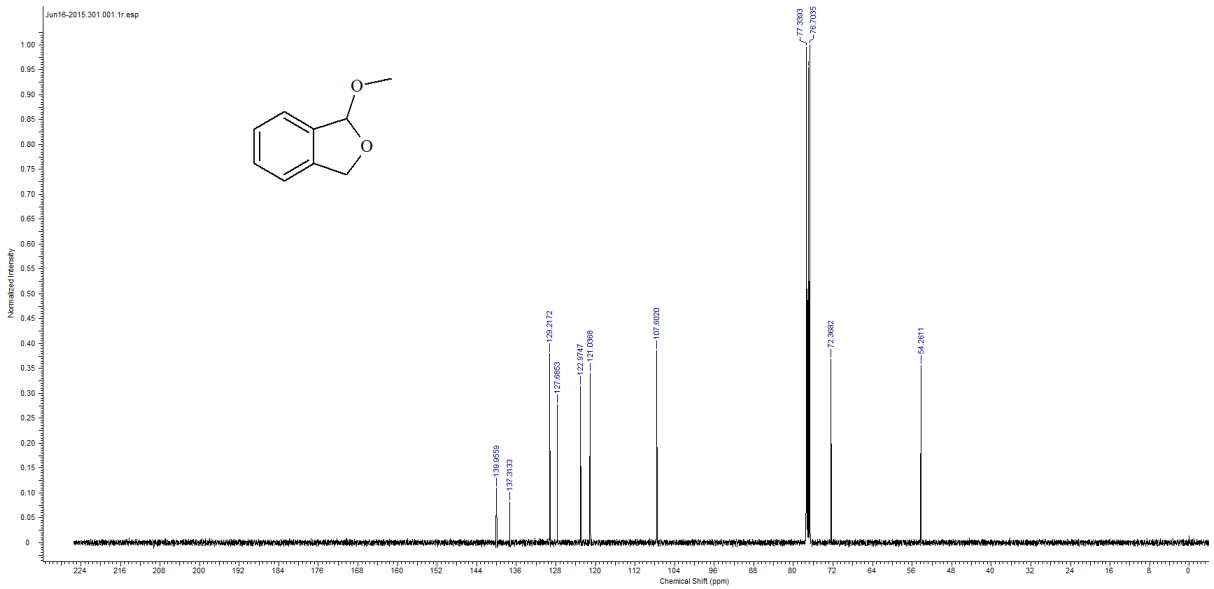

Jun03-2015.600.001.1r.esp
OH
N
Cl
8.2974
8.0383
8.0153
7.8695
7.8392
7.7298
7.5752
7.2959
4.9478
4.9336
2.3400
2.2546
2.2354
0.0000
1.01 1.00 1.00 1.00 1.00 1.00
2.06
1.01
Normalized Intensity
Chemical Shift (ppm)

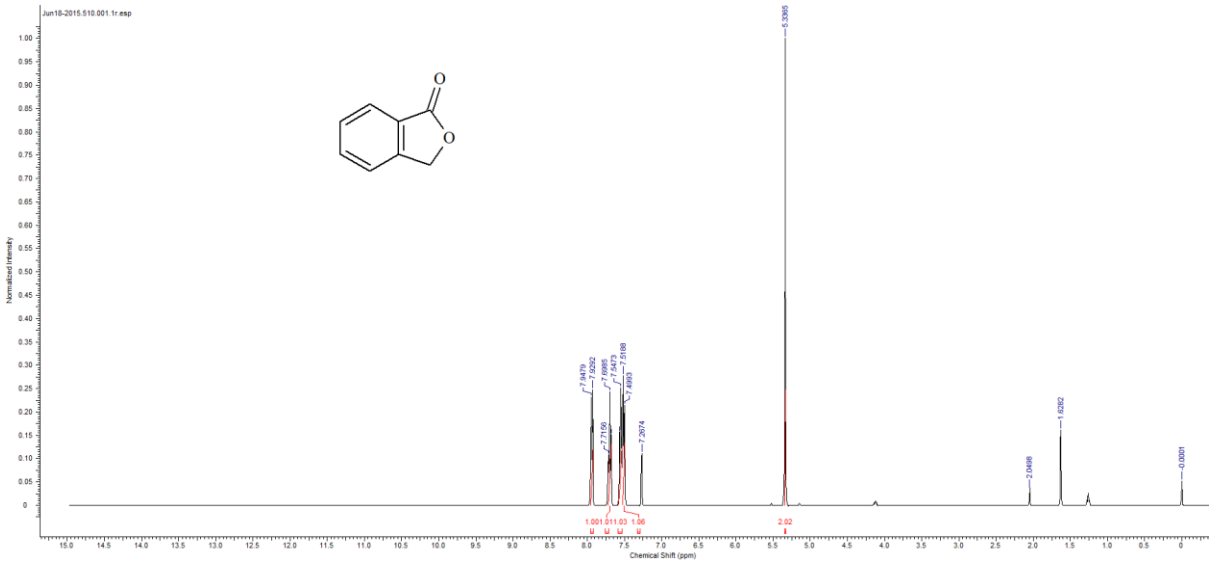

Jun03-2015.601.001.1r.esp
OH
N
Cl
77.3316
77.0176
76.6959
149.0784
146.9720
136.2410
132.3270
130.2599
128.2521
127.5928
127.2257
62.0986
Normalized Intensity
Chemical Shift (ppm)

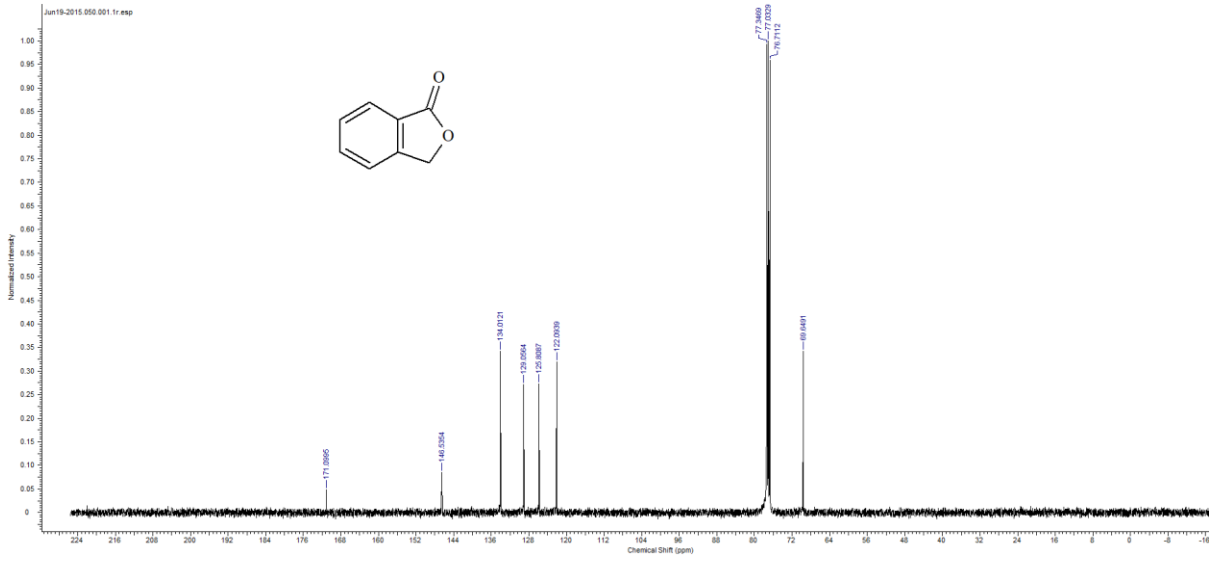

Jun09-2015.020.001.1r.esp
O
OH
N
Cl
Normalized Intensity
Chemical Shift (ppm)

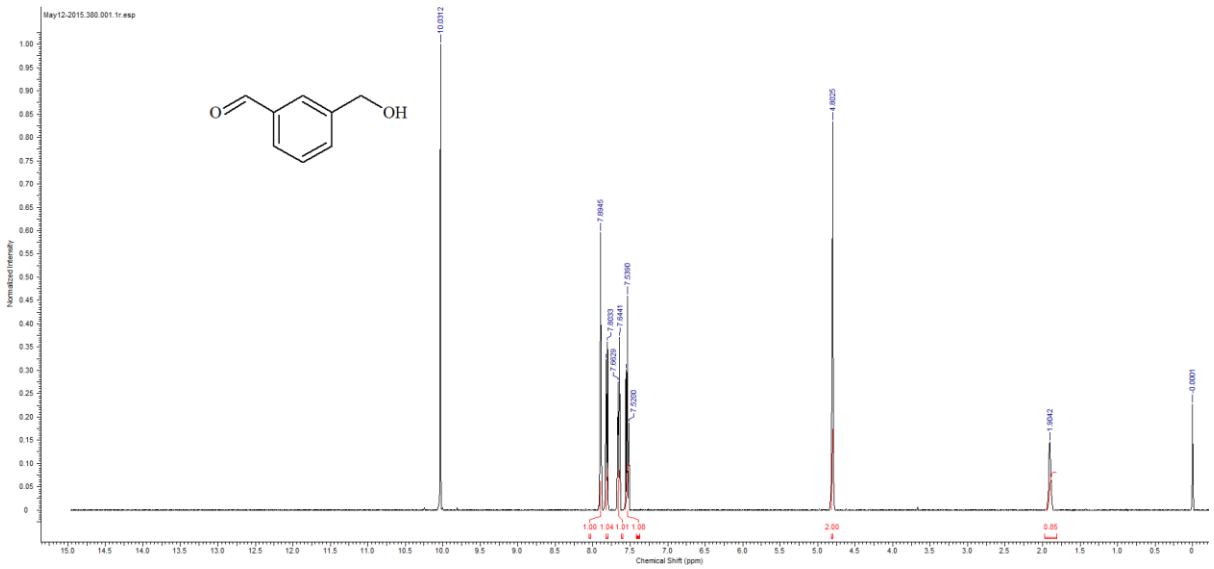

Jun10-2015.031.001.1r.esp
O
OH
N
Cl
Normalized Intensity
Chemical Shift (ppm)

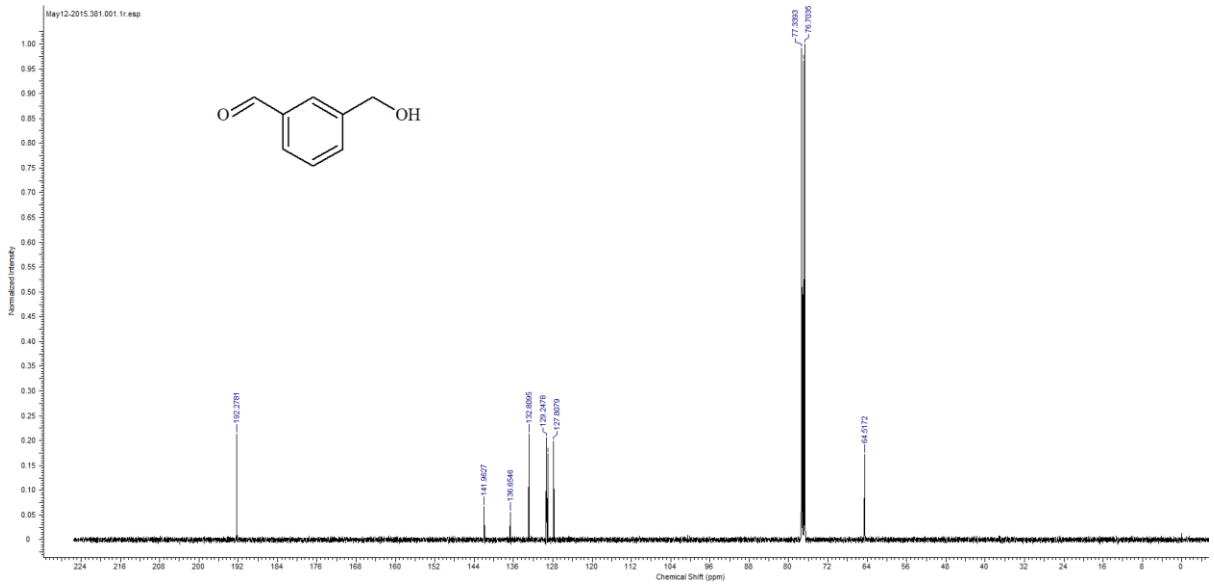

Jun16-2015.3003.001.1r.esp
O
O
Normalized Intensity
Chemical Shift (ppm)

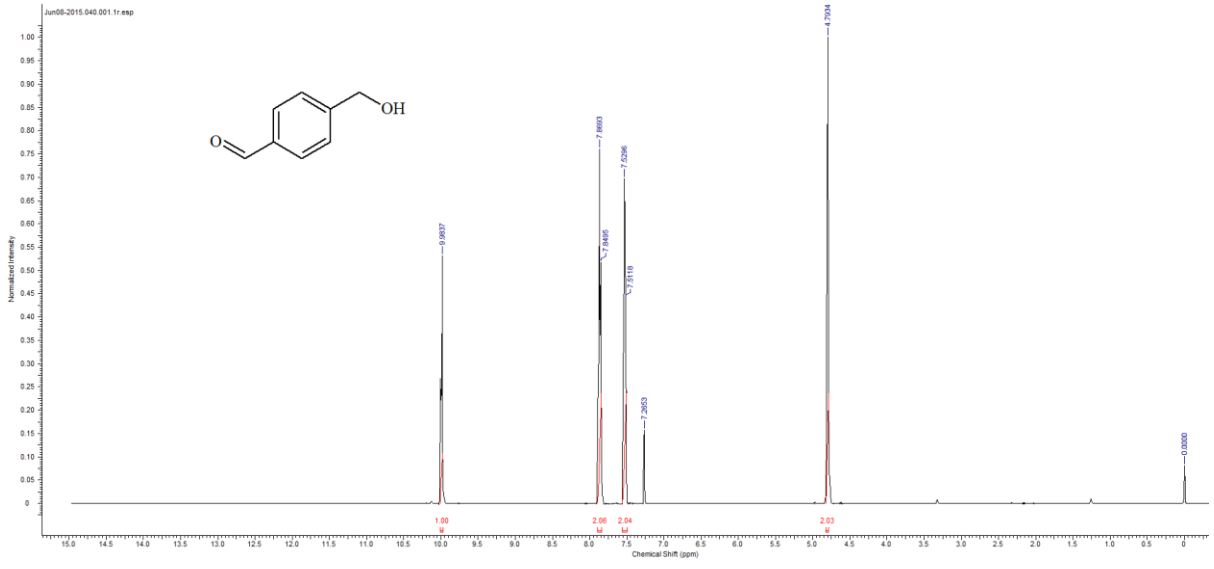

Jun16-2015.301.001.1r.esp
O
O
77.3393
76.7035
139.9659
137.3133
129.2172
127.6853
122.6747
121.0368
107.6020
72.3692
54.2611
Normalized Intensity
Chemical Shift (ppm)

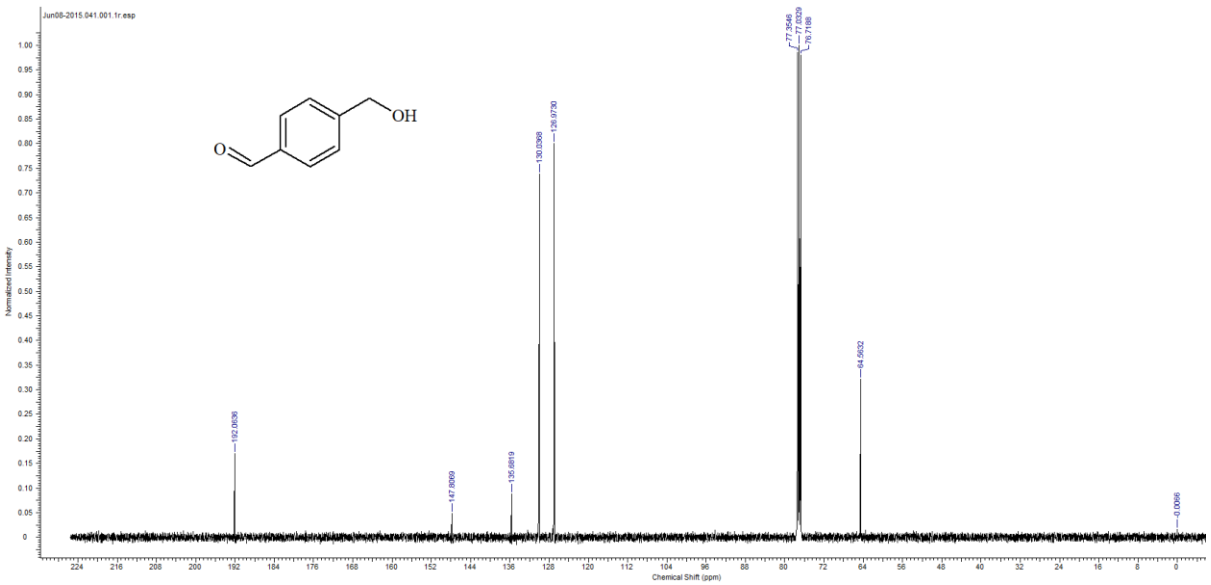

Jun18-2015.510.001.1r.esp
O
O
5.3365
7.9479
7.9362
7.6985
7.6473
7.5188
7.4993
7.3166
7.2674
2.0498
1.6262
0.0001
1.00
1.11
1.03
1.06
2.02
Normalized Intensity
Chemical Shift (ppm)

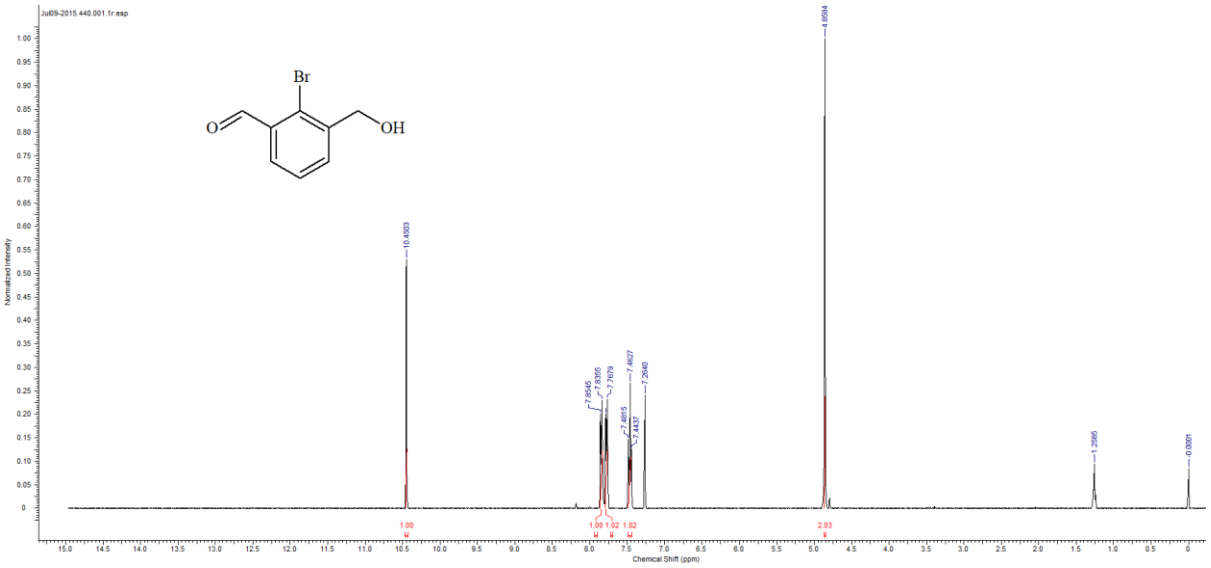

Jun19-2015.050.001.1r.esp
O
O
77.3469
77.0329
76.7172
134.0121
129.2564
125.8887
122.0039
69.6491
171.2995
146.5354
Normalized Intensity
Chemical Shift (ppm)

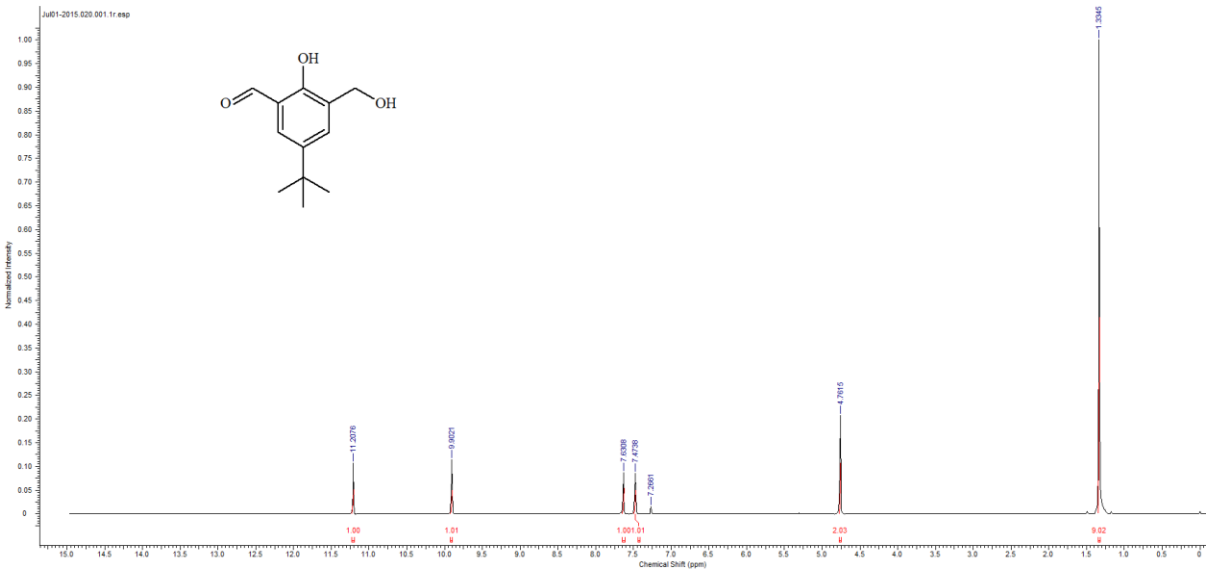

May12-2015.380.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
OH
10.0312
7.8945
7.8933
7.8929
7.8441
7.8390
7.6320
4.8825
1.9842
0.0001
1.00
1.04
1.01
1.08
2.00
0.85

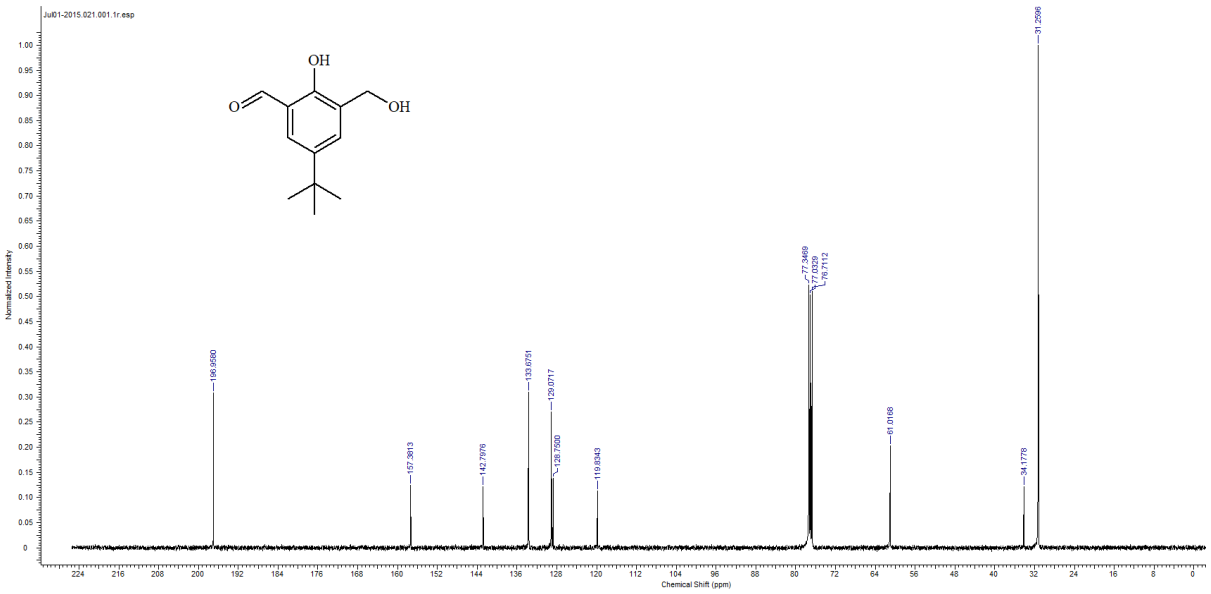

May12-2015.381.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
OH
192.2781
141.9627
136.6546
132.8066
129.2478
127.8079
77.3393
76.7035
64.5172

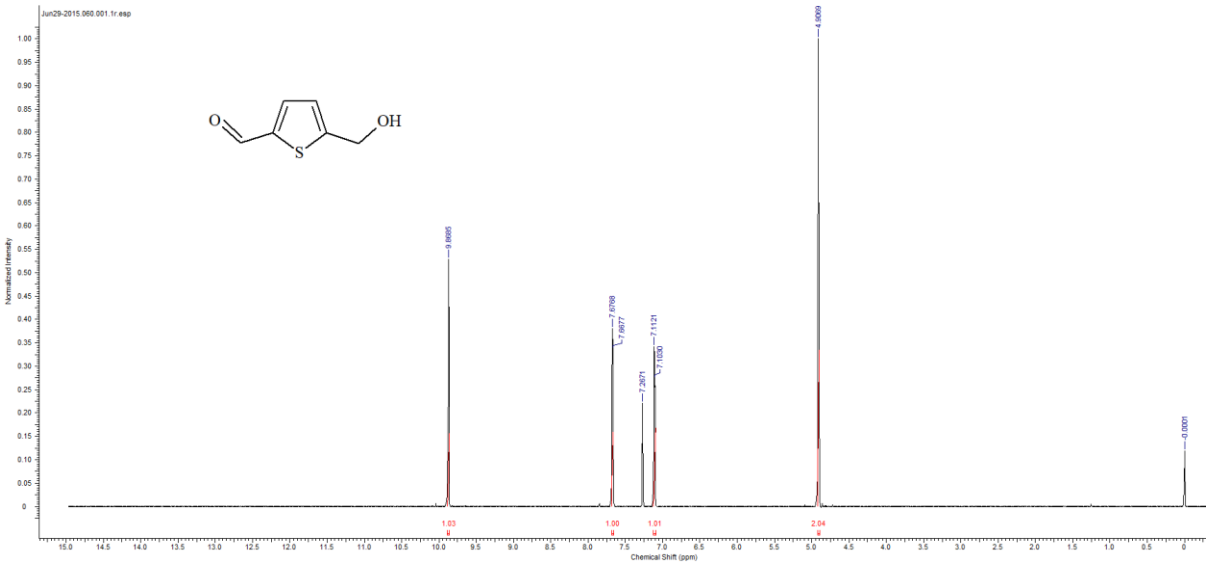

Jun08-2015.040.001.1r.esp
Normalized Intensity
Chemical Shift (ppm)
O
OH
9.9837
7.8693
7.5206
7.4495
7.3518
7.2953
4.7934
0.0000
1.00
2.06
2.04
2.03

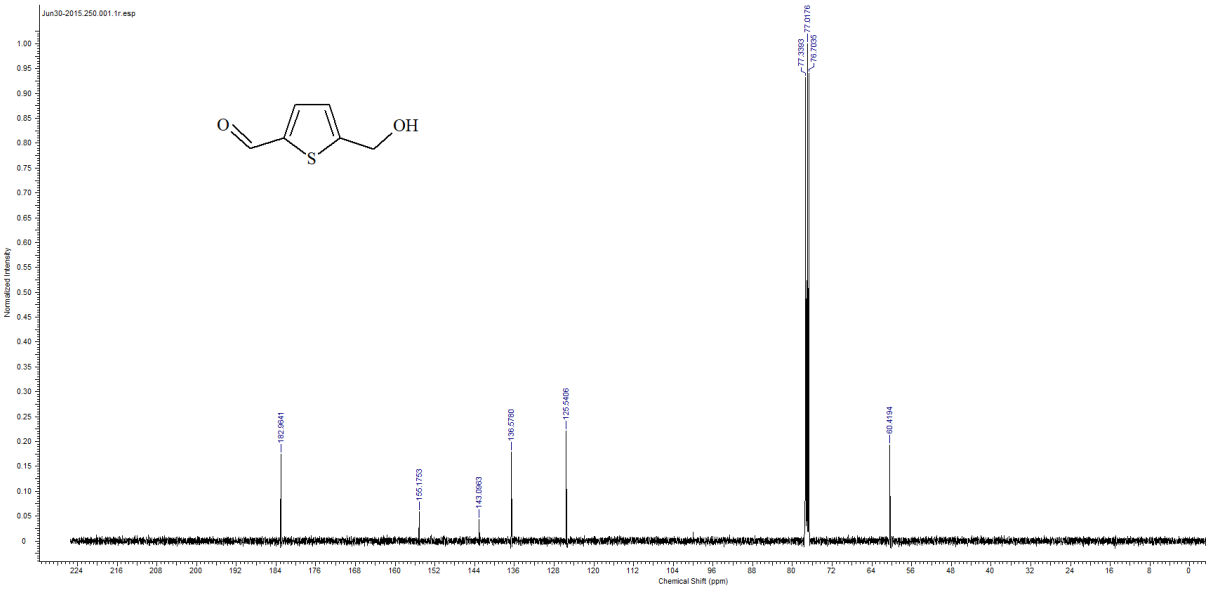

Jun08-2015.041.001.1r.esp
OH
O
192.0636
147.8069
135.6819
130.0368
126.9730
77.3546
77.0329
76.7188
64.5632
0.0066
Normalized Intensity
Chemical Shift (ppm)


Ju09-2015.440.001.1r.esp
Br
O
OH
10.4923
7.8545
7.8355
7.7679
7.4627
7.4615
7.4437
7.2640
4.8594
1.2985
0.0001
1.00
1.00
1.02
1.02
2.03
Normalized Intensity
Chemical Shift (ppm)


Ju01-2015.020.001.1r.esp
OH
O
OH
11.2076
9.9021
7.8398
7.4736
7.2661
4.7615
1.3045
1.00
1.01
1.001.01
2.03
9.02
Normalized Intensity
Chemical Shift (ppm)


Jul01-2015.021.001.1r.esp
OH
O
OH
Normalized Intensity
196.9580
157.3813
142.7976
133.6751
129.0717
128.7500
119.9343
77.3469
77.0329
76.7112
61.0188
34.1778
31.2596
Chemical Shift (ppm)


Jun29-2015.060.001.1r.esp
O
OH
S
Normalized Intensity
9.8885
7.8708
7.8677
7.3671
7.1121
7.1030
4.8809
3.0001
1.03
1.00
1.01
2.04
Chemical Shift (ppm)


Jun30-2015.250.001.1r.esp
O
OH
S
Normalized Intensity
192.9641
155.1753
143.0963
136.5760
125.5406
77.3383
77.0176
76.7035
60.4194
Chemical Shift (ppm)